"RISK STRATIFICATION OF PATIENTS WITH HYPERTROPHIC CARDIOMYOPATHY AND ASSESSMENT OF BIVENTRICULAR DIASTOLIC FUNCTION BY PULSE/TISSUE DOPPLER ECHOCARDIOGRAPHIC IMAGING"

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In partial fulfillment of the requirements for the award of the degree of

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CERTIFICATE

This is to certify that the dissertation entitled **"RISK STRATIFICATION OF PATIENTS WITH HYPERTROPHIC CARDIOMYOPATHY AND ASSESSMENT OF BIVENTRICULAR DIASTOLIC FUNCTION BY PULSE/TISSUE DOPPLER ECHOCARDIOGRAPHIC IMAGING"** is the bonafide original work of **Dr.A.MURALIDHARAN** in partial fulfillment of the requirements for D.M. Branch-II (CARDIOLOGY) examination of THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY to be held in August 2013.The period of post-graduate study and training was from August 2010 to July 2013.

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DECLARATION

I, **Dr.A.MURALIDHARAN,** solemnly declare that this dissertation entitled, **"RISK STRATIFICATION OF PATIENTS WITH HYPERTROPHIC CARDIOMYOPATHY AND ASSESSMENT OF BIVENTRICULAR DIASTOLIC FUNCTION BY PULSE/TISSUE DOPPLER ECHOCARDIOGRAPHIC IMAGING"** is a bonafide work done by me at the department of Cardiology, Madras Medical College and Government General Hospital during the period 2010 – 2013. under the guidance and supervision of the Professor and Head of the department of Cardiology of Madras Medical College and Government General Hospital, Professor **V.E.DHANDAPANI M.D.D.M.** This dissertation is submitted to The Tamil Nadu Dr.M.G.R Medical University, towards partial fulfilment of requirement for the award of **D.M. Degree (Branch-II) in Cardiology.**

Place : Chennai **Dr.A.MURALIDHARAN**
Date:

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INDEX

INTRODUCTION

Hypertrophic cardiomyopathy is a common autosomal dominant cardiovascular disease .

Dynamic obstruction to LV outflow can occur under resting or physiologically provocable conditions in patients with HCM. various phenotypic and genotypic heterogeneity are observed in HCM. HCM is the most common genetically transmitted cardiovascular disease which affects 1 in 500 people. The most frequent cause of sudden cardiac death in young athletes is HCM[1]. HCM patients may have very severe to negligible hypertrophy.HCM patients can have fibrosis and disarray of cardiac myocytes which may be minimal to extensive .

HCM patients have a natural history which may range from being aymptomatic to having protracted dyspnea and angina.

Sudden cardiac death may be the presenting event in some hypertrophic cardiomyopathy patients [2] . Hypertrophic cardiomyopathy was reported by Teare in 1958 as 'asymmetrical hypertrophy of the heart in young adults'[1].

The WHO defined cardiomyopathies as 'diseases of different and often unknown etiology in which the dominant feature is cardiomegaly and heart failure'[1]. In 1980 this definition was updated as 'heart muscles diseases of unknown cause'[1].This differentiated HCM from heart muscle diseases of known etiology, such as myocarditis.

Idiopathic hypertrophic subaortic stenosis, muscular subaortic stenosis have been the alternate old nomenclature for hypertrophic obstructive cardiomyopathy[2] .

In 1995, a WHO/International Society and Federation of Cardiology Task Force defined HCM as 'left and/or right ventricular hypertrophy, usually asymmetric and involving the interventricular septum with predominant autosomal dominant inheritance involving sarcomeric contractile proteins'[3].

AIM OF THE STUDY:

1.Risk stratification of patients with Hypertrophic Cardiomyopathy .

2.Assessment of Biventricular diastolic function in patients with Hypertrophic cardiomyopathy by pulse/tissue doppler echocardiographic imaging

REVIEW OF LITERATURE

HCM results by mutations encoding contractile proteins- β-myosin heavy chain and myosin binding protein C , troponin T and I, regulatory and essential myosin light chains, titin, α-tropomyosin, α-actin, α-myosin heavy chain, and muscle LIM protein [4].

The clinical manifestations vary among patients, from asymptomatic, to heart failure. Asymmetric hypertrophy of the interventricular septum, with or without left ventricular outflow tract obstruction is mostly diagnosed by echocardiography . We have to exclude other causes of hypertrophy, like hypertension, coarctation of aorta and aortic stenosis [5].

Athletes with physiological hypertrophy of left ventricle confound the diagnosis of HCM . The prevalence of HCM is 1:500 in young adults.

Genetic screening of all first degree relatives is recommended. Most of the Mutations in HCM happen as single nucleotide substitutions or "missense" mutations[5].

Pathology

Severe left ventricular hypertrophy and small LV size are gross features seen in HCM.

The ventricular septum is mainly hypertrophied.Hypertrophy may also be symmetrical or affect posterior wall, apex or middle part of the LV .Asians have a prevalence of about 10 % in midventricular obstruction.

Involvement of right ventricle can also be found in infants and children .End stage dilated cardiomyopathy is seen in 5% of patients with HCM. Dilated cardiomyopathy found in end stage of HCM has widespread fibrosis, heart wall thinning and LV dilation [6].

Raised LVEDP causes dilation of left atrium.Left atrium is also dilated by diastolic relaxation abnormalities and mitral insufficiency resulting from left ventricular outflow tract obstruction or related mitral valve abnormalities . The cause of mitral regurgitation in hypertrophic obstructive cardiomyopathy was originally ascribed to be due to the Venturi effect created by systolic flow acceleration in the left ventricular outflow tract pulling the anterior mitral leaflet of mitral valve towards the ventricular septum causing obstruction and regurgitation[7] .

A study suggested, that at the beginning of ejection the mitral valve leaflets are projecting into a narrow left ventricular outflow tract causing fast forward flow which is the main force that drags the leaflets toward the septum causing obstruction[8]. The systolic anterior motion of the mitral leaflets prevents the closing of mitral valve causing mitral insufficiency.

Differences between physiologic and pathologic hypertrophy

Left Ventricular Hypertrophy

Blood pressure and volume increase results in increase in muscle mass of heart.cardiac myocyte replication rate is not rapid, hence its mostly results by an enlargement in size of the cardiac myocyte than a rise in number .

During growth,pregnancy and in athlete's heart physiological hypertrophy occurs. Pathological cardiac hypertrophy occurs in hypertension. There are many differences among physiological and pathological myocyte hypertrophy LV hypertrophy is an adaptive reaction that helps the myocardium to preserve cardiac output [9]. Cardiac remodelling involves left ventricular dilation, accumulation of collagen and cardiac myocyte loss.

Athlete's heart is a form of physiologic cardiac hypertrophy which is not associated with fibrosis or dysfunction

Concentric and Eccentric myocyte Hypertrophy :

Physiological hypertrophy induced by exercise may be concentric or eccentric. Increased volume load of ventricle produces eccentric hypertrophy. Swimming and running are examples of endurance exercise which increase volume overload. In Eccentric cardiac hypertrophy there is a raise in the length of myocytes, which results in dilation of Left Ventricle.

Pressure overload causes concentric hypertrophy.There is left ventricle wall thickening and LV dilatation is mininal. Isometric exercises cause pressure overload .

Stimulus for Hypertrophy Resulting From Exercise :

Exercise results in the discharge of growth factors and neurotransmitters, which stimulate receptors on different cell types to cause a biological reaction.

Insulin-like growth factor 1 concentrations are increased in professional football players. IGF1 levels have a good correlation with LV mass index and LV end-diastolic dimension index[10].

During exercise norepinephrine a neurotransmitter is released. Norepinephrine levels did not have a correlation with thickness of left ventricle myocardium or LV cavity dimensions .Hence norepinephrine does not increase cardiac myocyte size

Stimuli For Pathological Hypertrophy

G Protein-Coupled Receptors

In cardiac failure patients Angiotensin II and endothelin-1 are upregulated. Heart myocytes release Angiotensin II and endothelin-1 during mechanical stress . Angiotensin II and endothelin-1 signal by combining to G protein-coupled receptors .

Calcineurin

The key enzyme involved in pathological hypertrophy is calcineurin.In patients with hypertrophy of LV and cardiac failure calcineurin activity is increased,

HCM- signalling pathways

In HCM signalling pathways have not been clearly defined. It has been suggested that Mutant proteins in HCM could stimulate hypertrophy by signalling pathways included in pressure overload type of hypertrophy.

Angiotensin II and endothelin I are increased in individuals with HCM.

Hypertrophy in HCM

Hypertrophy seen mostly marked in the area of the anterior papillary muscle and Superior part of septum.Systolic anterior motion of mitral leaflet causes dynamic obstruction in HCM. Increased afterload stress results from dynamic obstruction.

Genetically determined sarcomeric protein regional dysfunction causes abnormal stresses on nearby regions of normal myocardium..

Clinical findings

Cardiomegaly usually found on a chest x-ray, or electrocardiographic changes can be the initial presentation .Fatigue , breathlessness on exertion, palpitations, angina, syncope or sudden death may be the initial symptomology of presentation.

On physical examination, in pulse there is a rise and rapid descent. Bulge of precordium and outward displacement of apical impulse are present when there is cardiac enlargement. S4 causing a bifid apical impulse is frequently seen. Mid systolic murmur with

variable intensity is present in the left sternal border and apex .Pansystolic murmur of mitral regurgitation may be present at the apex

The midsystolic murmurs vary with maneuvers that result in increase or decrease left ventricle outflow gradient.

Softer Mid systolic murmurs along the left sternal border may be present in non-obstructive HCM also.The intensity of this murmur is softer. Atrial fibrillation occurs in endstage dilated hypertrophic cardiomyopathy. Wolff-Parkinson-White syndrome may be present in patients with hypertrophic cardiomyopathy rarely.

Sudden cardiac death can be the only presenting symptom in hypertrophic cardiomyopathy [11] .End stage is seen in about 5 % of patients with HCM and is characterized by systolic failure associated with left ventricular wall thinning and increased ventricular volume [12] .

Diastolic Dysfunction in HCM

Most of HCM patients have abnormalities in relaxation and filling.In diastole ,isovolumic relaxation stage is considerably lengthened and it causes a reduced rate and volume of filling. The contribution of atrial systole to ventricular filling is considerably increased[13].

Laboratory studies

Electrocardiogram

In nearly every individual with HCM there are electrocardiographic abnormalities seen. left ventricular hypertrophy can be assessed by voltage criteria and Left atrial enlargement can be seen. ST-T changes are present. Q waves which are pathological can be seen.

Wolff-Parkinson-White pattern or syndrome can be detected in electrocardiogram by the presence of delta wave.Genetic Mutations encoding AMP-activated protein kinase (*PRKAG2*) and lysosome associated membrane protein 2 are associated with WPW syndrome .

24 hour Holter monitoring and treadmill stress testing can be used for finding out arrhythmias and stratification of risk . Nonsustained ventricular tachycardia detected by 24 hrs Holter monitoring and a blood pressure response which is abnormal to treadmill testing are risk factors for sudden death[7].

Echocardiographic evaluation of HCM

For the diagnosis of hypertrophic cardiomyopathy echocardiography is a very important tool. The diagnosis can be established by

echocardiography,it is also very useful for followup and stratification of risk for sudden death. Probable or definite echocardiographic evidence of HCM is detected on the basis of recognition of a hypertrophied left ventricle with inter ventricular septum /posterior wall thickness ≥1.3 .When the right ventricular wall thickness exceeds 4 mm the right ventricle is considered to be involved too . Asymmetric left ventricular hypertrophy is the hallmark of HCM, the hypertrophy is more marked in the interventricular septum .Concentric hypertrophy has also been seen in some individuals. Apical hypertrophy and isolated hypertrophy of anterior wall or the mid part of left ventricle can also be seen. The mid ventricular obstruction may lead to the development of an apical left ventricular aneurysm.Left atrial enlargement can be seen due to result of mitral regurgitation and diastolic dysfunction. Systolic anterior motion of anterior mitral leaflet found in patients with hypertrophic obstructive cardiomyopathy is seen . Color flow Doppler allows to find the location of obstruction. Continuous wave Doppler can be used to find the left ventricular outflow tract gradient . The severity of Mitral regurgitation can be found out by continuous wave doppler. The primary mitral valve abnormalities are better detected by Transesophageal echocardiography .The primary mitral valve abnormalities can cause mitral regurgitation in patients with HCM.

When there is no resting gradient ,exercise Stress echo can be used to bring out the latent gradient in HCM . Doppler flow velocities across miral inflow and pulmonary vein can be used to find out diastolic dysfunction in hypertrophic cardiomyopathy .

For the detection of diastolic dysfunction in HCM ,tissue Doppler is very useful and more sensitive than pulse doppler .Using tissue Doppler we can detect HCM in carriers of the genetic mutation even before the development of hypertrophy

For identification of hypertrophic cardiomyopathy carriers reduced systolic and diastolic tissue doppler velocities have a high sensitivity and specificity

The prominent diastolic abnormality seen in patients with HCM is impaired LV relaxation . For the detection of high filling pressures, Mitral inflow and pulmonary venous flow assessments are not sensitive. LV filling pressure, peak E velocity of mitral inflow and mitral annular velocities (Ea) detected by tissue doppler have a good correlation.The realaxation abnormalities can be detected even before the start of hypertrophy in individuals with HCM . The response to septal ablation and surgery can be monitored by tissue doppler

Computed tomography and Cardiac MRI :

CT and Cardiac MRI are very useful when thoracic deformities prevent satisfactory cardiac visualization by transthoracic echocardiography. Cardiac MRI has also demonstrated that mitral leaflet elongation is present in hypertrophic cardiomyopathy independently of other phenotypic variants indicating that the mitral abnormalities are primary, thus, their important role in the pathophysiology of the obstruction in LVOT .

Gadolinium magnetic resonance imaging late enhancement allows detection of the amount of myocardial fibrosis and is a predictor of systolic dysfunction

Cardiac catheterization :

Cardiac catheterization helped in the initial understanding of the physiopathology of hypertrophic cardiomyopathy .Noninvasive imaging techniques like Doppler-echocardiography, computed tomography, and magnetic resonance imaging have replaced cardiac catheterization for diagnostic purposes. Nowadays, this method is only used before planned surgical treatment or percutaneous interventions for septal reduction.

Complications of HCM :

Main complications in children with HCM are syncope and sudden death. Sudden cardiac death may be initial presentation of the disease and is considered to be secondary to ventricular tachycardia and fibrillation caused by myocardial fibrosis and ischemia . Sudden death occurs more often in older children with hypertrophic cardiomyopathy either during strenuous sport activities or at rest but is infrequent in infants who are more prone to present and die with congestive heart failure specially in secondary forms .

Arrhythmias: Supraventricular and nonsustained ventricular tachycardias, were found in almost a third of pediatric and adolescent patients with hypertrophic cardiomyopathy studied by ambulatory electrocardiography Rarely, 3rd degree atrioventricular block is found in children with hypertrophic cardiomyopathy. They could present with near syncope or syncopal attacks as the first manifestation of the disease

Nonsustained ventricular tachycardia:

Most of the patients in this age group do not have nonsustained ventricular tachycardia in holter monitoring.Nonsustained ventricular tachycardia can be seen during 24 hrs holter monitoring in 20% to 30% of adults[14].

Evolving phenotype

Children with hypertrophic cardiomyopathy may evolve to dilated or restrictive cardiomyopathy phenotypes in 5% of the cases. In both circumstances they have a poor prognosis and become candidates for heart transplantation .

Infectious endocarditis

Infectious endocarditis is a rare complication in hypertrophic cardiomyopathy Infectious endocarditis can affect the anterior mitral valve leaflet in the ventricular side.

Stroke

Ischemic stroke is somewhat frequent and a cause of death in adult hypertrophic cardiomyopathy but has not been seen in children .

Medical treatment in HCM:

Beta-blockers and verapamil are used on an empirical basis. Most physicians use beta-blockers as the firstline drug in the treatment of HCM.Verapamil is not preferred as the initial drug.

Beta-blockers or verapamil do not have evidence for prevention of sudden cardiac death.

Symptom relief can be seen in most of patients who are on beta-blockers or verapamil.Medical therapy is used for only symptomatic patients.Medical therapy cannot be used prophylactically.

Surgery in HCM :

Surgical indication for patients with HCM are a very high gradient, severe symptoms and failure of drug treatment .Myectomy has become the primary option for these patients.five to ten grams of muscle are resected from tha basal septum by surgery.

The LVOT gradient is reduced in more than 90% of patients and provides symptomatic improvement in functional status[15].

DDD pacing to relieve LVOT obstruction

DDD pacing with shortened A-V delay was used to reduce the outflow gradient and improve quality of life in patients with HCM who are failures of medical treatment. The mechanism of action causing this lowering of left ventricular outflow gradient is not known. Several trials have found out that DDD pacing is not effective in the treatment of HCM[16].They have suggested only a placebo role in the symptomatic improvement seen in patients who have been treated with DDD pacing. Now DDD pacing is not recommended for treatment of patients with obstructive HCM.

Alcohol septal ablation :

The first septal artery when temporarily occluded by an angioplasty balloon caused a reduction in LVOT gradient. This formed the basis for alcohol septal ablation as a treatment option for HCM[17].Contrast echocardiography is utilised for assessing the perfusion bed supplied by first septal artery and it is marked out and it predicts the infarct size following alcohol injection.

RISK STRATIFICATION IN HCM

Hypertrophic cardiomyopathy is the most frequent etiology of sudden cardiac death in young . Male preponderance is seen among athletes .

The primary prevention risk factors for SCD in HCM include family history of SCD, unexplained recent syncope, runs of nonsustained ventricular tachycardia on 24 hrs Holter monitoring, hypotensive response to exercise and maximum left ventricular wall thickness greater than 30 mm[18] .

Sustained ventricular tachycardia and ventricular fibrillation are the most important causes of SCD . Increased SCD risk is caused due to excess sympathetic activation during exercise.

SUDDEN CARDIAC DEATH PREVENTIVE MEASURES IN HCM

Betablockers and verapamil do not prevent sudden cardiac death in hypertrophic cardiomyopathy

Implantation of ICD is the most effective procedure to prevent sudden cardiac death in HCM. ICD is primarily used for secondary prevention and in primary prevention of sudden cardiac death in HCM and this has been proved in many studies[19].

ICD implantation in HCM is a class I indication for secondary prevention and classIIB for primary prevention as given in guidelines of AHA/ACC/NASPE [20].

The disadvantage of ICD is its high cost.History of prior cardiac arrest or spontaneous sustained ventricular tachycardia in patients is a mandatory indication for ICD implantation.

For primary prevention of sudden cardiac death in children, ICD implantation is not preferred.Amiodarone can be used as bridge to ICD implantation in children till they reach adulthood.

MATERIALS AND METHODS

This was a retrospective cross-sectional study done between March 2012 and March 2013 at the department of cardiology, Government General Hospital Chennai. The study cohort comprises 40 patients with Hypertrophic cardiomyopathy who are referred to the department of cardiology, for evaluation or follow up.

SETTING : **Department of Cardiology, Rajiv Gandhi Government General,**

Madras Medical College, Chennai.

- ❖ DESIGN OF STUDY : Prospective observational study
- ❖ PERIOD OF STUDY : 1 Year
- ❖ SAMPLE SIZE : 40

INCLUSION CRITERIA

- Probable or definite echocardiographic evidence of HCM on the basis of recognition of a hypertrophied left ventricle with inter ventricular septum /posterior wall thickness ≥1.3

EXCLUSION CRITERIA

1) Non-diagnostic echocardiographic studies

2) Other concomitant loading or systemic conditions that may lead to left ventricular hypertrophy -Systemic hypertension ,Aortic stenosis,Coarctation, or Structural LVOT obstruction

3) HCM patients who have undergone surgical or catheter septal myectomy

STUDY PROCEDURE

All patients referred for echocardiography during this period were included.

1) 2D, M-mode,Pulseand Tissue Doppler measurements taken.

2) Diastolic function of both Left ventricle and Right ventricle evaluated.

3) Detecting and grading of the systolic anterior motion of the mitral valve, LV outflow tract obstruction, intracavitary obstruction and mitral regurgitation assessed.

4) Describing the pattern of left ventricular hypertrophy

DATA COLLECTION and ANALYSIS

- Interviewer will administer the proforma. Past medical history and relevant history will be collected as per hospital record after explaining aim of the study & getting written consent

- Demographic data such as age, gender, and clinical presentation; ECG data and echocardiographic data will be described and analysed.

- Echocardiography done on Philips HD7XE machine .

- 24 hour HOLTER study done for patients.

ECHOCARDIOGRAPHIC EVALUATION OF BIVENTRICULAR DIASTOLIC FUNCTION IN HCM

Transthoracic Echocardiography was performed in all hypertrophic cardiomyopathy patients with Philips HD7XE machine .

Interventricular septum thickness, left ventricular posterior wall thickness, left ventricular end diastolic diameter, left ventricular end systolic diameter, right ventricular free wall thickness, right ventricular end diastolic diameter, fractional shortening of left ventricle were the variables assessed .

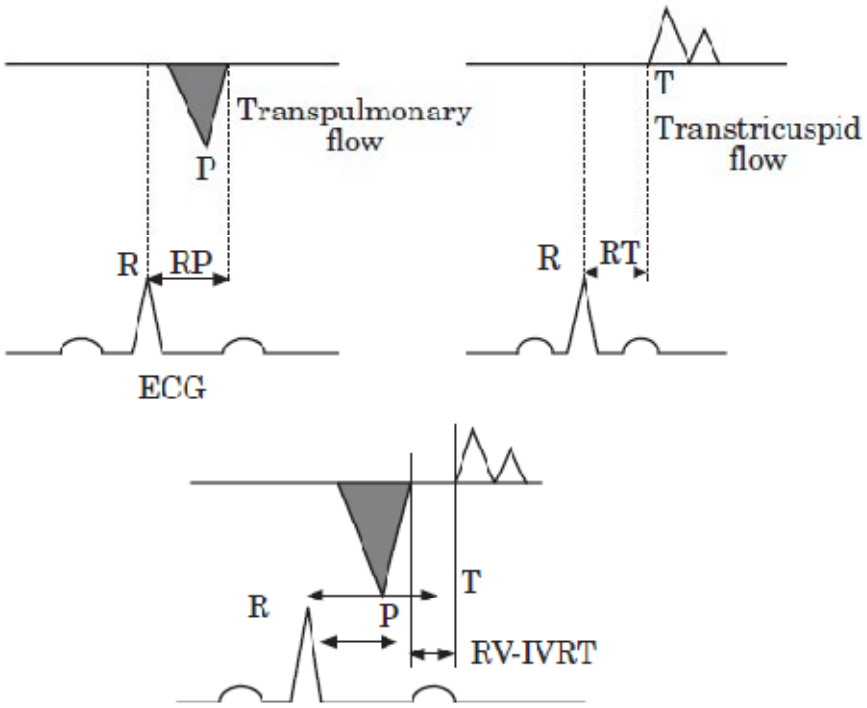
The left ventricular diastolic function was determined from the transmitral pulse doppler inflow patterns taken from the apical four-chamber view by positioning sample volume at the tips of the mitral leaflets during diastole.

Right ventricular diastolic function was assessed from the apical 4 chamber view by sample volume at the tips of tricuspid leaflets during diastole.

peak velocity of E wave of tricuspid inflow , peak velocity of A wave of tricuspid inflow, E/A ratio, deceleration time of E wave and right ventricular isovolumic relaxation time were calculated for assessment of right ventricular diastolic function.

TISSUE DOPPLER IMAGING

The tissue doppler velocity of myocardium was measured at septal side of mitral valve annulus to determine Septal mitral annular tissue Doppler velocity MV Ea and MV Aa . The tissue doppler velocity of myocardium was measured at lateral side of tricuspid valve annulus to determine lateral tricuspid annular tissue Doppler velocity TV Ea and TVAa. In our study the patients were divided into two groups according to their left ventricular outflow gradient gradient less than 30 mmHg were the non-obstructive HCM group, and LV outflow gradient more than 30 mmhg were the obstructive HCM group.



CLASSIFICATION OF HCM PATIENTS ACCORDING TO MARON SUBTYPES[21]

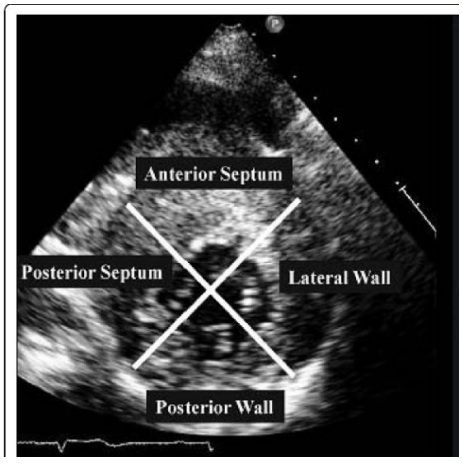
Type I : Hypertrophy confined to the anterior portion of the ventricular septum.

Type II : Hypertrophy involving the anterior and posterior septum

Type III : Hypertrophy involving the anterior and posterior septum as well as the lateral free wall.

Type IV :Hypertrophy involving left ventricular regions other than the anterior septum and the posterior free wall

- using short-axis view the left ventricle is divided in 4 LV wall segments: anterior and posterior septum and posterior and lateral wall Segments are visualized at mitral and papillary level.
- possible extension to the apex is visualized by 4 chamber view



Statistical Analysis

All the obtained data were analyzed by Medcalc software.Continuous data are expressed as mean values ± SD.Student's t-test was used to assess the significant differences of mean values between patients with non-obstructive and obstructive HCM. A p-value ≤0.05 was considered statistically significant.

Pearson correlation coefficient was used to assess the correlation between right Ventricle and left ventricle diastolic parameters.

RESULTS

TABLE 1 : BASELINE CHARACTERISTICS OF STUDY-(n = 40) PATIENTS

MALE/FEMALE	31/9
AGE	41.8 ±10.7
SYMPTOMS	
BOE	18 (45%)
PALPITATION	22 (55%)
ANGINA	22 (55%)
SYNCOPE	21 (52.5%)
FAMILY H/O SCD	11 (27.5%)
HOLTER-NSVT	10 (25%)
MARON CLASSIFICATION	
TYPE I	3 (7.5%)
TYPE II	6 (15%)
TYPE III	15 (37.5%)
TYPE 1V	16 (40 %)
TYPE V	0
LVEDD (mm)	42.1± 4.4
LVESD (mm)	24.1 ±3.8
FS (%)	41.7± 7.9
OBSTRUCTIVE HCM-LVOTG > 30 mm Hg	13 (32.5%)
SAM	
GRADE 1	4 (10%)
GRADE II	6 (15%)
GRADE III	3 (7.5%)
GRADE IV	0
MITRAL REGURGITATION	
GRADE 1	5 (12.5%)
GRADE II	8 (20%)
GRADE III	0
GRADE IV	0

The study cohort comprises 40 consecutive patients with Hypertrophic cardiomyopathy who were referred to our department for evaluation or follow up. There were 31 male and 9 female patients in our study.

Mean age (± SD) was 41.8 years (± 10.7), for males 43.3 (± 9.6) yrs, and for females 36.7 (± 13.5) yrs.

TABLE 2 : AGE DISTRIBUTION

AGE	N = 40 (%)
20-29	4 (10 %)
30-39	13 (32.5 %)
40-49	12 (30 %)
50-59	8 (20 %)
60-69	3 (7.5 %)
TOTAL	40

10 % of patients were in 20-29 years age group.32.5 % of patients were in 30-39 years age group.30% of patients were in 40-49 years age group.20% of patients were in 50-59 years age group.7.5% of patients were in 60-69 years age group

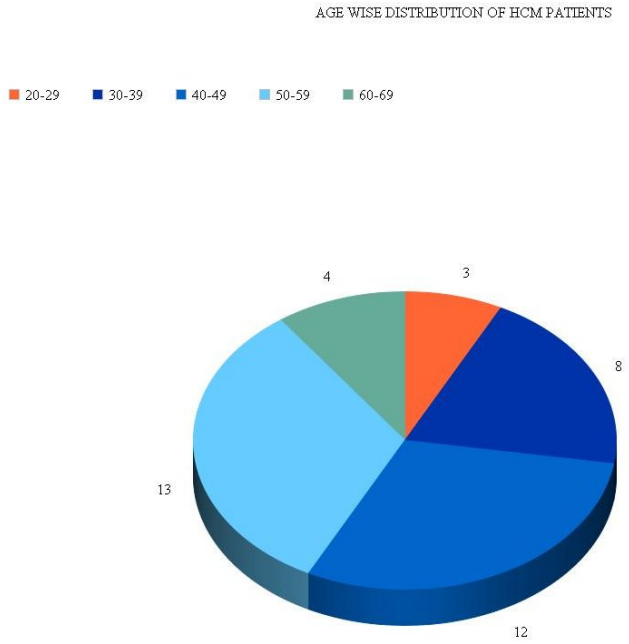


FIGURE 1

TABLE 3: AGE DISTRIBUTION ACCORDING TO MARON TYPES

TYPE	NO (%)	AGE (YRS)
I	3 (7.5 %)	49 ± 6.5
II	6 (15%)	38 ± 8.8
III	15 (37.5 %)	42.1± 11.2
IV	16 (40 %)	41.6 ±11
TOTAL	40	41.8 ± 10.7

Mean age (± SD) of Maron type I patients were 49 ± 6.5 years. Mean age (± SD) of Maron type II patients were 38 ± 8.8 years. Mean age (± SD) of Maron type III patients were 42.1± 11.2 years. Mean age (± SD) of Maron type IV patients were 41.6 ± 11.2 years .

TABLE 4: FREQUENCY ACCORDING TO TYPES IN MARONS CLASSIFICATION

TYPE	**N0 (%)**
I	3 (7.5 %)
II	6 (15%)
III	15 (37.5 %)
IV	16 (40 %)
V	Nil
TOTAL	40

The patients were categorized according to the Maron types of HCM. 7.5 % of patients were in type I.15 % of patients were in type II. 40 % of patients were in type IV and 37.5% patients were in type III Maron . There were no patients with type V (apical HCM) Maron.

FIGURE 2 :N0 OF PTS ACCORDING TO MARON TYPES

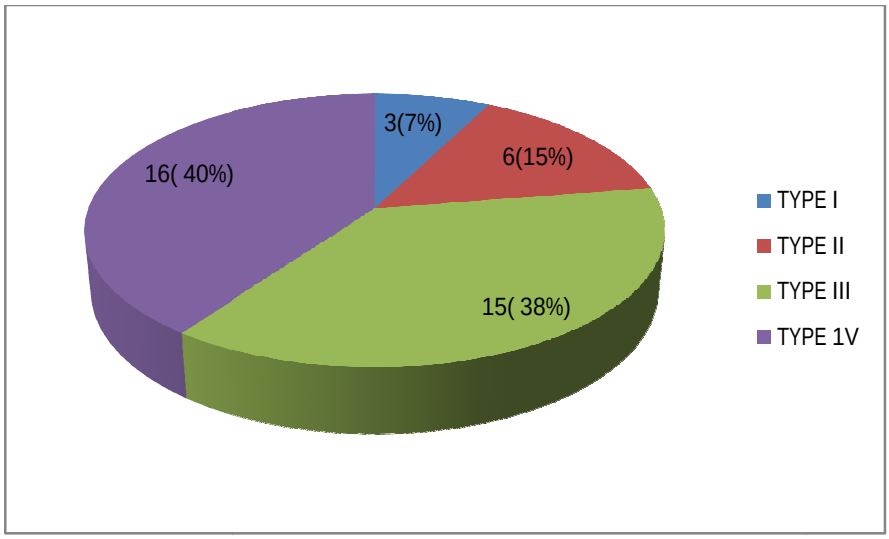


TABLE 5 : CATEGORIZATION OF OBSTRUCTIVE HCM ACCORDING TO MARON TYPES

TYPE	NO (%)	NO OF OBSTRUCTIVE TYPE
1	3 (7.5 %)	0
II	6 (15%)	0
111	15 (37.5 %)	7 (46.7%)
1V	16 (40 %)	6 (40%)
TOTAL	40 (100%)	13 (32.5%)

Left ventricular obstruction

No obstruction was found in 27 (67.5%) patients. 32.5 % of patients had obstructive HCM (>30 mmHg LV outflow obstruction) was found in 13 (32.5 %) cases,with a rest gradient mean(+SD) of 65 (± 31.5) mmHg.

46.7 % of Maron type III HCM patients had obstructive HCM and 40% of Maron type IV HCM patients had obstructive HCM

FIGURE 3:CATEGORIZATION OF OBSTRUCTIVE AND NONOBSTRUCTIVE HCM BY MARON TYPES

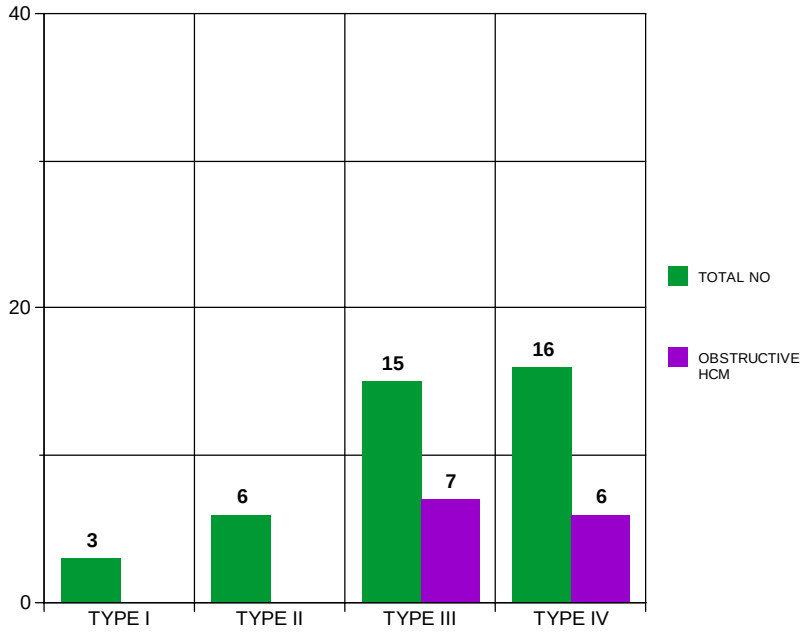
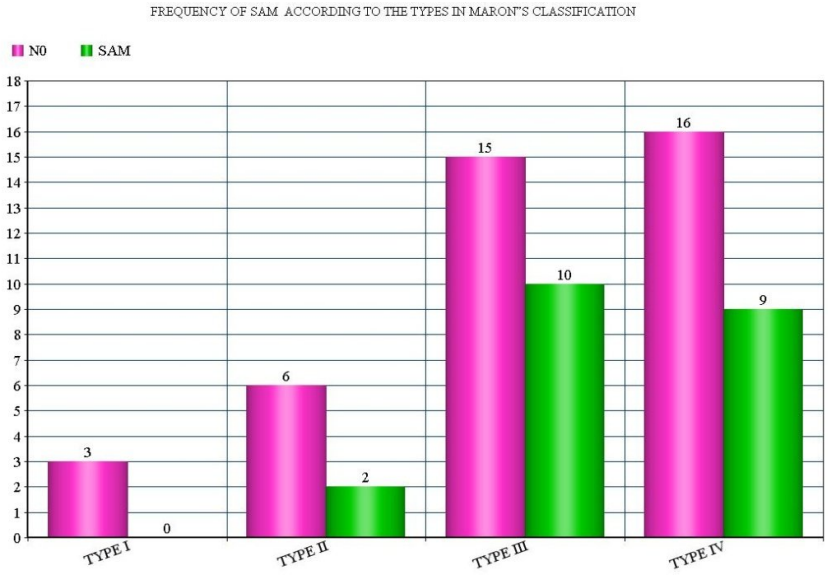


TABLE 6 FREQUENCY OF SAM ACCORDING TO THE TYPES IN MARON"S CLASSIFICATION

TYPE	NO (%)	NO OF SAM (%)
1	3 (7.5 %)	0
II	6 (15%)	2 (33.3%)
111	15 (37.5 %)	10(66.7%)
1V	16 (40 %)	9 (56.25%)
TOTAL	40 (100%)	21 (52.5%)

FIGURE 4:



No patients in Maron Type I HCM had Systolic anterior motion of mitral leaflet (SAM).66.7 % OF Type III and 56.25 % of type IV HCM had SAM.

TABLE 7 : SEPTUM AND LVPW THICKNESS ACCORDING TO MARON TYPES

TYPE	SEPTUM (mm)	LVPW(mm)
I	20.1 ± 2.1	9.1 ± 0.9
II	18.6 ± 2.4	9.5 ± 0.5
III	15.9 ± 2.9	8.5 ± 1.3
IV	16.9 ± 2.8	9.2 ± 1.8
TOTAL	17.3 ± 2.3	8.9± 1.4

FIGURE 5:COMPARISION OF SEPTAL THICKNESS ACCORDING TO MARON TYPES OF HCM

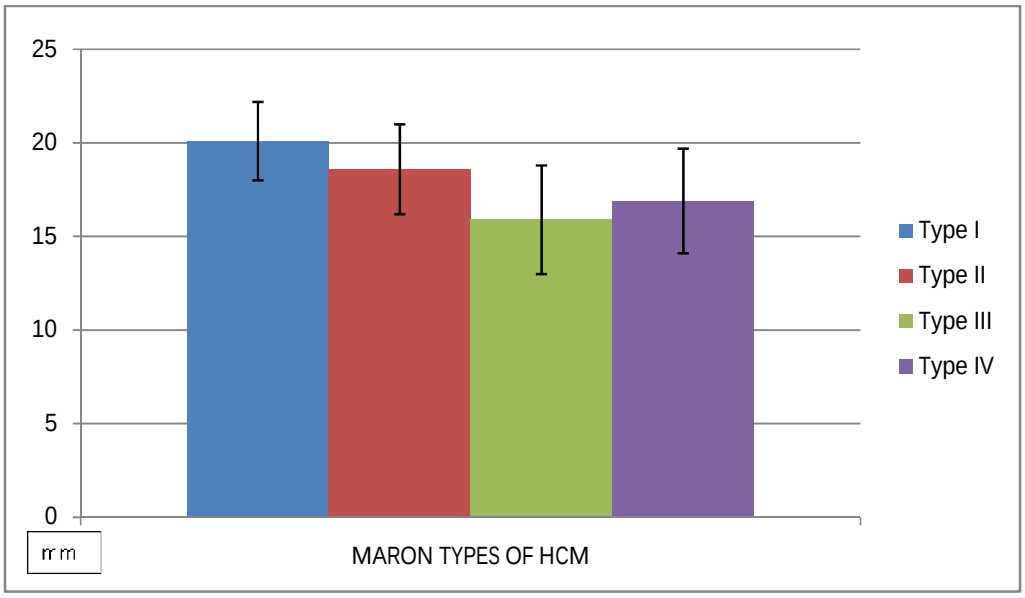
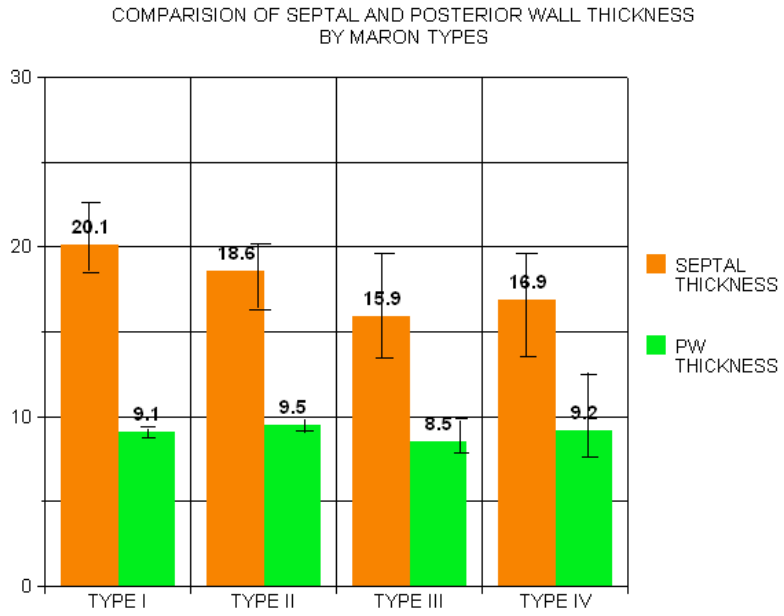


FIGURE 6:



The maximum septal thickness was 21.8 mm. The mean septal thickness and (±SD) was 17.3 (±2.3) mm.

The maximum LV posterior wall dimension was 12 mm. The mean LV posterior wall thickness(±SD) was 8.9 (±1.4) mm

The mean septal thickness and (±SD) of Maron type I was 20.1 (± 2.1) mm. The mean septal thickness and (±SD) of Maron type II was 18.6 (± 2.4) mm. The mean septal thickness and (±SD) of Maron type III was 15.9 (± 2.9) mm. The mean septal thickness and (±SD) of Maron type IV was 16.9 (± 2.8) mm.

TABLE 8 :CATEGORIZATION OF MITRAL INFLOW VELOCITIES ACCORDING TO MARON TYPES

TYPE	LV-PV E (cm/s)	LV-PVA(cm/s)	LV-DTE (msec)
I	53.2 ± 8.2	53.2± 17.2	256± 14.7
II	79.1± 16.5	58.8 ± 11.3	162.3 ± 45
III	74.5± 24.8	82.4 ± 34.9	186.6±47.7
IV	107.2±42.5	69 ± 17.6	155 ± 31.9
TOTAL	86.6±35.3	71.3 ± 26	175.5 ± 46.6

The mean (± SD) of peak velocity E of mitral inflow velocity of all patients is 86.6±35.3 cm/s.The mean (± SD) of peak velocity A of mitral inflow velocity of all patients is 71.3 ± 26 cm/s.

The mean (± SD) of peak velocity E of mitral inflow velocity of type I Maron HCM patients is 53.2 ± 8.2 cm/s . The mean (± SD) of peak velocity A of mitral inflow velocity of type I Maron HCM patients is 53.2± 17.2 cm/s.

The mean (± SD) of peak velocity E of mitral inflow velocity of type II Maron HCM patients is 79.1± 16.5 cm/s. The mean (± SD) of peak velocity A of mitral inflow velocity of type II Maron HCM patients is 58.8 ± 11.3 cm/s

The mean (± SD) of peak velocity E of mitral inflow velocity of type III Maron HCM patients is 74.5± 24.8 cm/s. The mean (± SD) of peak velocity A of mitral inflow velocity of type III Maron HCM patients is 82.4 ± 34.9 cm/s.

The mean (± SD) of peak velocity E of mitral inflow velocity of type IV Maron HCM patients is107.2±42.5 cm/s. The mean (± SD) of peak velocity A of mitral inflow velocity of type IV Maron HCM patients is 69 ± 17.6 cm/s.

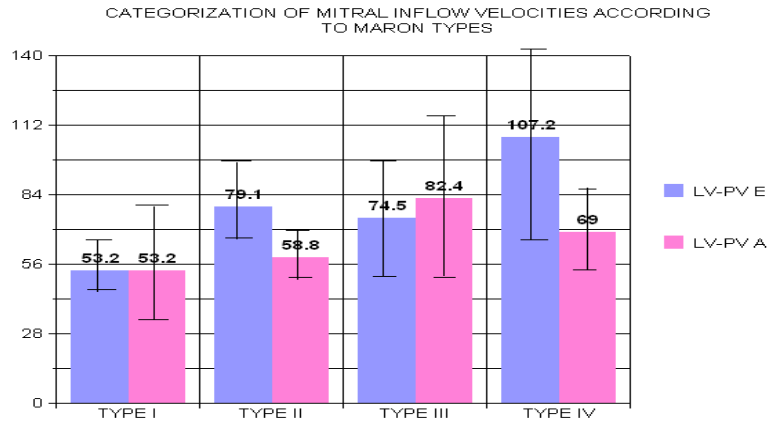
The mean (± SD) of deceleration time of mitral inflow E velocity in all patients is 175.5 ± 46.6 msec.

The mean (± SD) of deceleration time of mitral inflow E velocity in type I Maron is 256± 14.7 msec. The mean (± SD) of deceleration time of mitral inflow E velocity in type II Maron is 162.3 ± 45 msec. The mean (± SD) of deceleration time of mitral inflow E velocity in type III Maron is 186.6±47.7 msec. The mean (± SD) of deceleration time of mitral inflow E velocity in type IV Maron is 155 ± 31.9 msec.

TABLE 9 :CATEGORIZATION OF TRICUSPID INFLOW VELOCITIES ACCORDING TO MARON TYPES

TYPE	RV-PV E(cm/s)	RV-PV A(cm/s)	RV-DTE (msec)
I	41.8 ±1	42.3 ± 6.9	161.7 ± 55.5
II	56.9 ±12.7	43.7 ±7.1	203 ± 63.4
III	50 ± 11.7	46.2 ± 10.6	221.8 ± 60.4
IV	60.4± 13.6	46.7 ±22.7	193.6 ±60.4
TOTAL	54.6 ±13.1	45.7± 15.6	203.3± 60.6

FIGURE 7



The mean (± SD) of peak velocity E of tricuspid inflow velocity of all patients is 54.6±13.1 cm/s.The mean (± SD) of peak velocity A of tricuspid inflow velocity of all patients is 45.7 ± 15.6 cm/s.

The mean (± SD) of peak velocity E of tricuspid inflow velocity of type I Maron HCM patients is 41.8 ± 1 cm/s . The mean (± SD) of peak velocity A of tricuspid inflow velocity of type I Maron HCM patients is 42.3± 6.9 cm/s.

The mean (± SD) of peak velocity E of tricuspid inflow velocity of type II Maron HCM patients is 56.9± 12.7 cm/s. The mean (± SD) of peak velocity A of tricuspid inflow velocity of type II Maron HCM patients is 43.7± 7.1 cm/s

The mean (± SD) of peak velocity E of tricuspid inflow velocity of type III Maron HCM patients is 50± 11.7 cm/s. The mean (± SD) of peak velocity A of tricuspid inflow velocity of type III Maron HCM patients is 46.2 ± 10.6 cm/s.

The mean (± SD) of peak velocity E of tricuspid inflow velocity of type IV Maron HCM patients is 60.4± 13.6 cm/s. The mean (± SD) of peak velocity A of tricuspid inflow velocity of type IV Maron HCM patients is 46.7 ± 22.7 cm/s.

The mean (± SD) of deceleration time of tricuspid inflow E velocity in all patients is 203.3± 60.6 msec.

The mean (± SD) of deceleration time of tricuspid inflow E velocity in type I Maron is 161.7 ± 55.5 msec. The mean (± SD) of deceleration time of tricuspid inflow E velocity in type II Maron is 203 ± 63.4msec. The mean (± SD) of deceleration time of tricuspid inflow E velocity in type III Maron is 221.8 ± 60.4msec. The mean (± SD) of deceleration time of tricuspid inflow E velocity in type IV Maron is 193.6 ±60.4 msec.

FIGURE 8

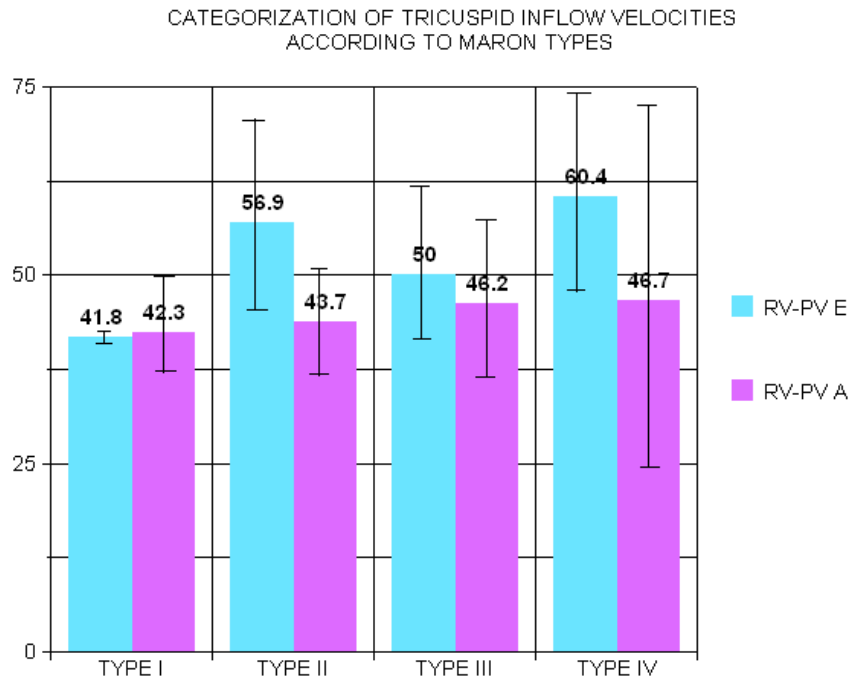
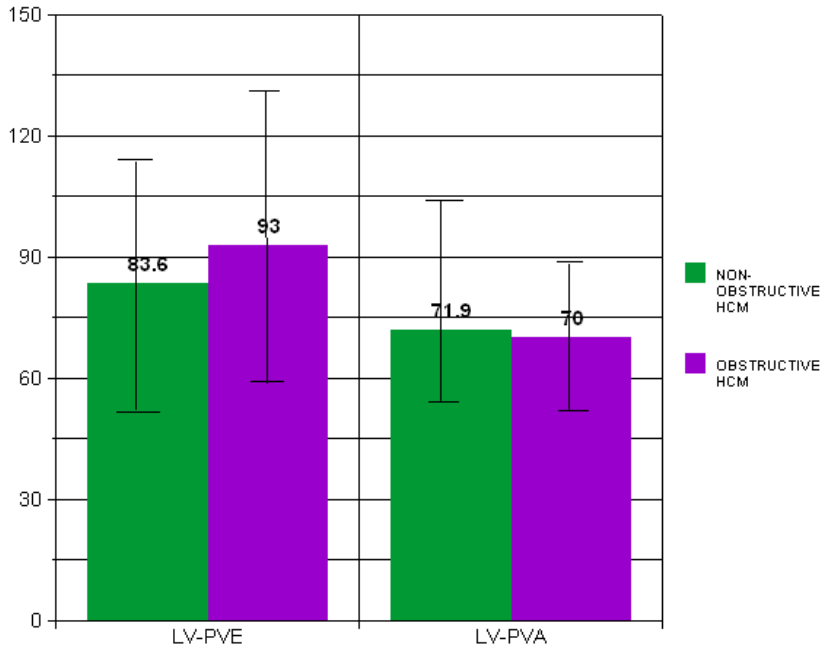


TABLE 10 : CHARACTERISTICS OF MITRAL INFLOW VELOCITIES BETWEEN NON-OBSTRUCTIVE AND OBSTRUCTIVE HCM

	NON-OBSTRUCTIVE (n=27)	OBSTRUCTIVE (n = 13)	P value
LV-PVE	83.6 ± 32.5	93 ± 39.9	0.43
LV-PV A	71.9 ± 28.5	70 ± 19.6	0.82
LV-DTE	179.6±48.9	167.1 ±40	0.42
LVOT GRADIENT	6.8 ± 4.2	65± 31.5	<0.0001

FIGURE 9 CHARACTERISTICS OF MITRAL INFLOW VELOCITIES BETWEEN NON-OBSTRUCTIVE AND OBSTRUCTIVE HCM



The mean (± SD) of peak velocity E of mitral inflow velocity of patients with non-obstructive HCM is 83.6 ± 32.5 cm/s.The mean (± SD) of peak velocity A of mitral inflow velocity of patients with non-obstructive HCM is 71.9 ± 28.5 cm/s. The mean (± SD) of deceleration time of mitral inflow E velocity in non-obstructive HCM is 179.6±48.9 msec.

The mean (± SD) of peak velocity E of mitral inflow velocity of patients with obstructive HCM is 93 ± 39.9 cm/s.The mean (± SD) of peak velocity A of mitral inflow velocity of patients with obstructive HCM is 70 ± 19.6 cm/s. The mean (± SD) of deceleration time of mitral inflow E velocity in patients with obstructive HCM is 167.1 ±40 msec. There was no significant statistical difference in mitral and tricuspid inflow velocities between non-obstructive and obstructive HCM.

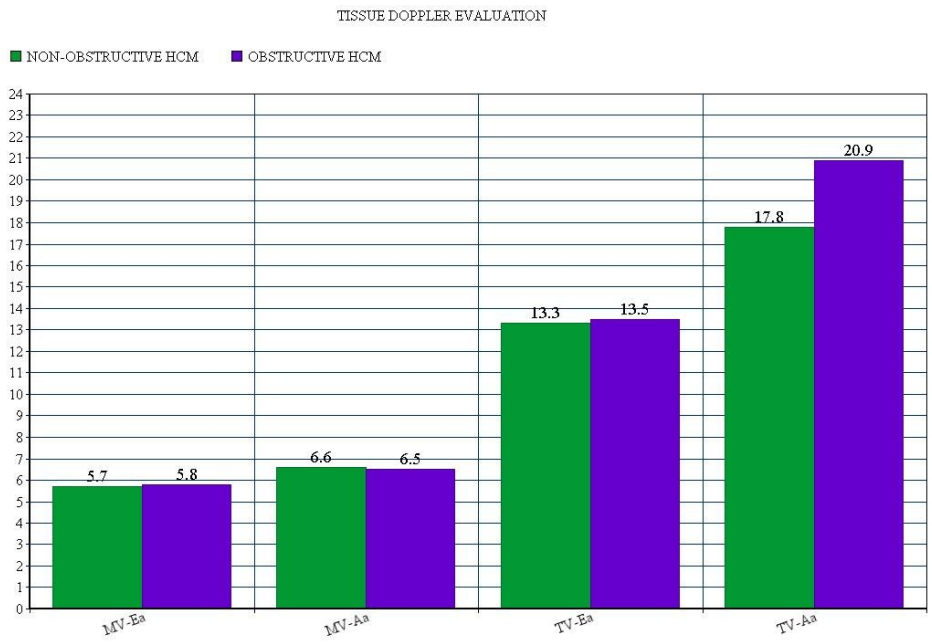
TABLE 11. Tissue Doppler Imaging velocities in patients with Hypertrophic cardiomyopathy

	Patients (n = 40) cm/s
MV Ea (septal)	5.8 ±2.4
MV Aa (septal)	6.5 ± 1.8
TV Ea (lateral)	13.4 ± 7.9
TV Aa (lateral)	18.8 ± 10.1

TABLE 12 Comparison the results of Tissue doppler velocities according to left ventricle outflow gradient

	NON-OBSTRUCTIVE (n=27)	OBSTRUCTIVE (n=13)	p-value
MV Ea (septal)	5.7± 2.3	5.8 ±2.7	0.9
MV Aa (septal)	6.6± 1.9	6.5± 1.8	0.87
TV Ea (lateral)	13.3± 7.6	13.5± 8.4	0.94
TV Aa (lateral)	17.8± 9.6	20.9± 10.7	0.36

FIGURE 10 : Comparison the results of Tissue doppler velocities according to left ventricle outflow gradient



All myocardial tissue Doppler velocities are decreased in the patients with HCM in comparison to the normal values.

Septal mitral annular tissue Doppler velocity MV Ea (septal) has a mean of 5.8 cm/s (±SD 2.4). MV Aa (septal) has a mean of 6.5 cm/s (± SD 1.8). Tricuspid annular tissue Doppler velocity TV Ea (lateral) has a mean of 13.4 cm/s (± SD 7.9).TV Aa (lateral) has a mean of 18.8 cm/s (± SD 10.1)

Septal mitral annular tissue Doppler velocity MV Ea (septal) in non-obstructive HCM has a mean of 5.7 cm/s (±SD 2.3). MV Aa (septal) has a mean of 6.6 cm/s (± SD 1.9). Tricuspid annular tissue Doppler velocity in non-obstructive HCM TV Ea (lateral) has a mean of 13.5 cm/s (± SD 8.4).TV Aa (lateral) has a mean of 17.8 cm/s (± SD 9.6).Septal mitral annular tissue Doppler velocity MV Ea (septal) in obstructive HCM has a mean of 5.8 cm/s (±SD 2.7). MV Aa (septal) has a mean of 6.5 cm/s (± SD 1.8). Tricuspid annular tissue Doppler velocity in obstructive HCM TV Ea (lateral) has a mean of 13.3 cm/s (± SD 7.6).TV Aa (lateral) has a mean of 20.9 cm/s (± SD 10.7)

There was no significant statistical difference in mitral and tricuspid tissue doppler velocities between non-obstructive and obstructive HCM.

TABLE 13 CORRELATION BETWEEN RV AND LV DIASTOLIC PARAMETERS

	LV-E/A	LV-DTE
RV-E/A	r = 0.36 p = 0.02	r = 0.34 p=0.03
RV-DTE	r = -0.32 p=0.04	r = 0.1 p=0.5

Correlation between RV and LV diastolic parameters were tested using pearson Correlation coefficient.There is significant correlation between right ventricle E/A ratio and left ventricle E/A ratio and left ventricular deceleration time of E wave. There is also significant correlation between right ventricle deceleration time of E wave and left ventricle E/A ratio.

FIGURE 11

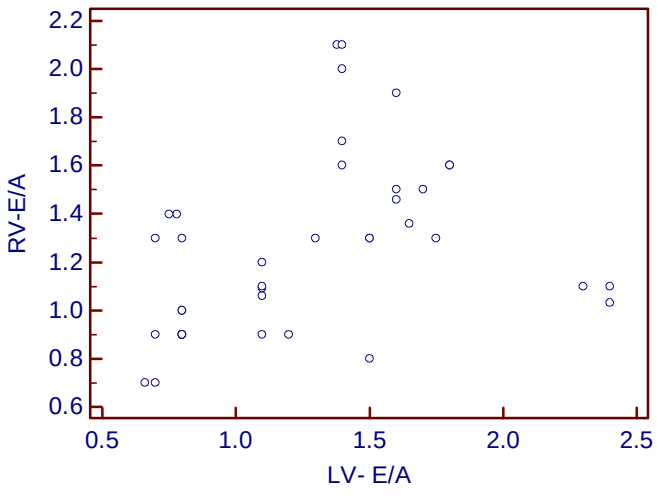
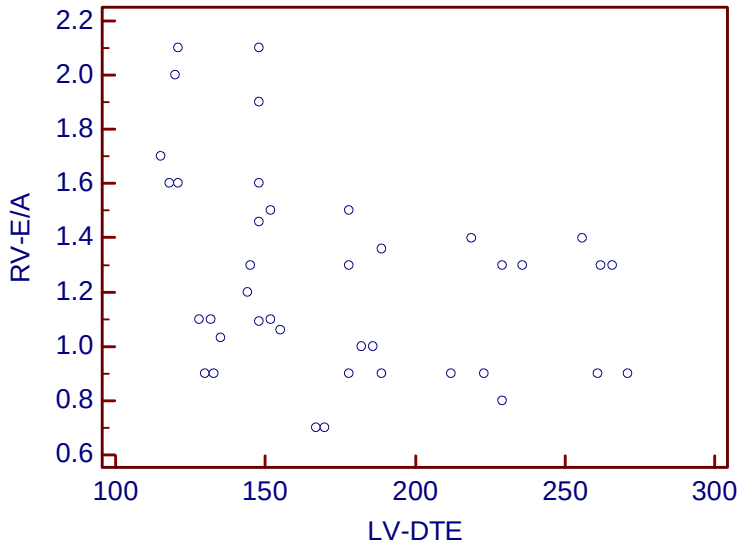


FIGURE 12:



There was no significant correlation between right ventricle deceleration time of E wave and left ventricle deceleration time of E wave.There was no significant correlation between tissue Doppler velocities of right ventricle and left ventricle.There was no significant correlation between right ventricle pulse and tissue Doppler parameters and septal wall thickness,right ventricle free wall thickness

TABLE 14: CLINICAL MANIFESTATIONS ACCORDING TO TYPES IN MARONS CLASSIFICATION

TYPE	No.	SYMPTOMS	BOE	PALPITATION	SYNCOPE	CHESTPAIN
I	3 (7.5 %)	2 (66.7%)		1(33.3%)	2 (66.7%)	
II	6 (15%)	5 (83.3%)	2 (33.3%)	3 (50%)	4 (66.7%)	
III	15 (37.5 %)	15 (100%)	7 (46.7%)	10 (66.7%)	6 (40%)	12 (80%)
IV	16 (40 %)	16 (100%)	9 (56.25%)	8 (50%)	9 (56.25%)	10 (62.5%)
TOTAL	40	37 (92.5%)	18 (45%)	22(55%)	21(52.5%)	22(55%)

92.5 % of patients with HCM had symptoms . chest pain and palpitation were present in 55 % of patients.Syncope was seen in 52.5% of patients. 45% of patients had breathlessness on exertion (BOE).66.7 % of patients with Maron Type I HCM had symptoms of which 66.7 % had syncope and 33.3 % of patients had palpitation.83.3 % of patients with Maron Type II HCM had symptoms of which 66.7 % had syncope , 50 % of patients had palpitation and 33.3% had breathlessness on exertion (BOE).All the patients with Maron Type III HCM had

symptoms of which 66.7 % had palpitation, 80 % of patients had chest pain,40 % of patients had syncope and 46.7 % had breathlessness on exertion (BOE).All the patients with Maron Type IV HCM had symptoms of which 50 % had palpitation, 62.5% of patients had chest pain,56.25 % of patients had syncope and breathlessness on exertion (BOE).

TABLE 15:RISK STRATIFICATION OF HCM ACCORDING TO MARON TYPES

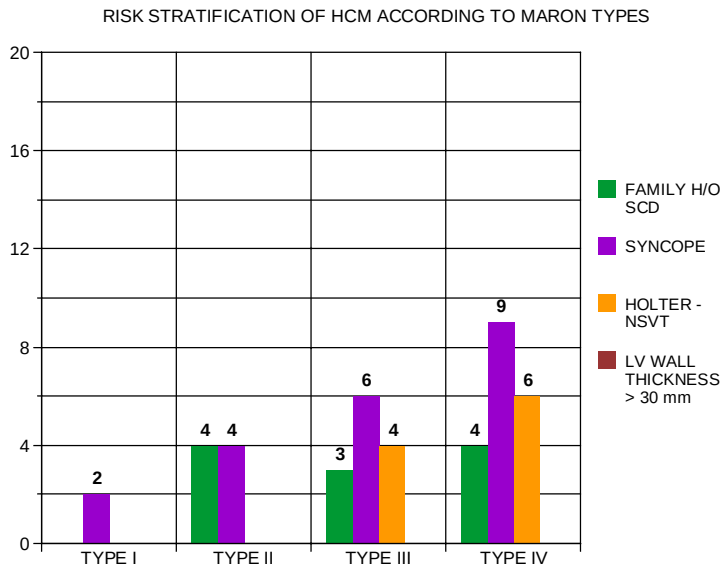
TYPE		FAMILY H/O SCD	LV WALL THICKNESS > 30 mm	SYNCOPE	HOLTER –NSVT
I	3 (7.5 %)	0	0	2 (66.7%)	0
II	6 (15%)	4 (66.7%)	0	4 (66.7%)	0
III	15 (37.5 %)	3 (20%)	0	6 (40%)	4(26.7%)
IV	16 (40 %)	4 (25%)	0	9 (56.25%)	6(37.5%)
TOTAL	40	11(27.5%)	0	21(52.5%)	10 (25%)

Family H/O sudden cardiac death was present in 27.5% of patients with HCM.66.7% of patients with Maron Type II had a family history of sudden cardiac death.20% of patients with Maron Type III had a family history of sudden cardiac death and 25 % of patients with Maron Type II had a family history of sudden cardiac death.

No patient had a maximum LV wall thickness of greater than 30 mm. Non-sustained ventricular tachycardia as detected by 24hrs Holter study was present in 25% of patients with HCM. Non-sustained ventricular tachycardia as detected by 24hrs Holter study was present in 26.7% of type III Maron HCM patients.. Non-sustained ventricular tachycardia as detected by 24hrs Holter study was present in 37.5 % of type IV Maron HCM patients.

Syncope was seen in 52.5% of all patients with HCM. Syncope was seen in 66.7% of patients with Maron Type I and II. Syncope was seen in 40 % of patients with Maron Type III and 56.25% patients with Maron type IV.

FIGURE 13



DISCUSSION

The prevalence of HCM in the adult general population is about 0.2% (1:500) based on several epidemiological studies[21,22]. Many patients having the mutant gene for HCM can go undetected clinically. Our study patients were those referred for echocardiography to our cardiology OPD.Our study is not a community screening study .Therefore one would expect it to underestimate the phenotypic prevalence in the community. The population harbouring the genetic defect is also underestimated.

Similar prevalence of HCM was found in no more than 1% of outpatients in Other studies which had patients as referrals to hospital[22].

The prevalence in females was significantly less than expected. Male prevalence ranged from 55% to 78% in previous studies[23,24].

There were 31 male and 9 female patients in our study.The female population is significantly lower in our study.only 22.5% of the study patients were female.

Reduced patient awareness[26],lesser indications for medical screening programs[25,27], and referral bias of clinicians[26] or clinical presentation which is delayed, which can result from genetic and

endocrine factors affecting expression of phenotype of the disease. Estrogens may have a protective effect on development of secondary hypertrophy[28,29] .

The nature of the study population was predominantly male in our study.

32.5 % of patients were in the 30-39 years age group and 30% were in the 40-49 years age group.Hence majority of patients studied in our study were in the 30-49 years age group.

our population were younger (mean age 41.8 ± 10.7 yrs) and it is to be noted that male predominance were seen from adolescence to mid-life in different studies.

Presence of LVOT obstruction in HCM

For categorization of HCM patients into different groups various cutoff based on LV outlow gradient and site of hypertrophy have been used. Strict categorization into different categories according to LV outflow gradient is difficult because of the unpredictability of dynamic changes that may occur in different patients. In our study we used 30 mmHg as a rest cut-off and /or a 50 mmnHg as a provocative induced LV outflow gradient. No obstruction was found in twenty seven (67.5%)

patients. Thirteen (32.5 %) of patients had obstructive HCM (>30 mmHg LV outflow obstruction) was found in 13 (32.5 %) cases,with a rest gradient mean(+SD) of 65 (± 31.5) mmHg.

46.7 % of Maron type III HCM patients had obstructive HCM and 40% of Maron type IV HCM patients had obstructive HCM .There was no obstructive HCM in Maron type I and II.

LV outflow obstruction prevalence have been from 23 – 77% in different studies[30-32]. Patients with obstructive HCM were older than other groups. Many of our patients where on medical therapy which may account for the low gradient in them.

LV hypertrophy patterns :

The classification of the left ventricular hypertrophy pattern in HCM has not been universally formalised. The most commonly used is the Maron classification[21].

The patients in our study were categorized according to the Maron types of HCM.

7.5 % of patients were in type I.15 % of patients were in type II. 40 % of patients were in type IV and 37.5% patients were in type III Maron .

There were no patients with type V (apical HCM) Maron.Type IV Maron was the predominant group in our study,which is in contrast to other studies were type III Maron was the predominant group[21].

The four patterns of Maron types of LV hypertrophy showed no difference in age. 92.5 % of patients with HCM had symptoms . chest pain and palpitation were present in 55 % of patients.Syncope was seen in 52.5% of patients. 45% of patients had breathlessness on exertion (BOE).

66.7 % of patients with Maron Type I HCM had symptoms of which 66.7 % had syncope and 33.3 % of patients had palpitation.83.3 % of patients with Maron Type II HCM had symptoms of which 66.7 % had syncope , 50 % of patients had palpitation and 33.3% had breathlessness on exertion (BOE).

All the patients with Maron Type III HCM had symptoms of which 66.7 % had palpitation, 80 % of patients had chest pain,40 % of patients had syncope and 46.7 % had breathlessness on exertion (BOE).

All the patients with Maron Type IV HCM had symptoms of which 50 % had palpitation, 62.5% of patients had chest pain,56.25 % of patients had syncope and breathlessness on exertion (BOE).

Syncope was present in all groups.The prevalence of syncope was higher in Maron type I and II.Majority of patients had chestpain in type III and IV. Chest pain as a symptom was not seen in type I and II.

Biventricular diastolic dysfunction in HCM

As shown in table 8 & 9, all myocardial velocities decreased in the patients with HCM in comparison to the normal values. Recent studies have shown that tissue doppler is a reliable method for early detection of HCM in genotype-positive patients before the onset of hypertrophy. Reduction in systolic and diastolic Tissue doppler velocities have been shown in various studies to have a high sensitivity and specificity for identifying mutation in HCM carriers.

Serial echocardiographic evaluation of patients with clinically normal phenotype but carrying the mutation of HCM have shown reduction in tissue doppler velocities and development of hypertrophy and diastolic dysfunction during follow up after many years.Impaired LV relaxation is a prominent diastolic abnormality in patients with HCM. Mitral inflow and pulmonary venous pulse Doppler flow assessments may not be sensitive for the detection of high filling pressures of the left ventricle. Simultaneous echocardiographic and invasive homodynamic studies have revealed no significant correlation

between mitral inflow or pulmonary venous flow parameters and filling pressures in patients with LV systolic dysfunction.Good correlation between LV filling pressure, mitral inflow E velocity, and tissue Doppler MV annular velocities (Ea) have been observed in studies.

All myocardial tissue Doppler velocities are decreased in the patients with HCM in comparison to the normal values in our study.Reduced tissue doppler early diastolic velocities that have been detected in our study indicate that diastolic abnormalities may precede the onset of hypertrophy in HCM.

Patients in Type IV showed maximum peak velocity of E in mitral inflow velocities. Patients in Type III showed maximum peak velocity of A in mitral inflow velocities.Deceleration time of Mitral inflow E velocity was maximum in Maron Type I HCM patients.Patients in Type IV showed maximum peak velocity of E and A in tricuspid inflow velocities. Deceleration time of tricuspid inflow E velocity was maximum in Maron Type III HCM patients.There was no statistically significant relationship between myocardial tissue Doppler velocities of obstructive and non-obstructive HCM.This is in contrast to a study by Rezvaneh Salehi et al which has observed positive correlation between reduced mitral annular Ea septal tissue Doppler velocity and LVOT gradient .

In all our study patients right ventricular diastolic function is impaired, with prolonged isovolumic relaxation time, prolonged deceleration time of E wave reversed E/A ratio and reduced tricuspid annular tissue Doppler velocities.

Different studies using cardiac MRI have found out diastolic bnormalities of the right ventricle like reduced rate of early filling and increased late filling in patients with HCM.

The observations in our study indicate that both left and right ventricles exhibit similarities in abnormal diastolic filling patterns. Left ventricular and right ventricular diastolic abnormalities are not related to the magnitude and severity of left and right ventricular hypertrophy respectively in our study.

A study by Spirito et al has observed that abnormalities in left ventricular relaxation in hypertrophic cardiomyopathy patients is not related to the proportion and severity of left ventricular hypertrophy[32].

The possible explanation for right ventricular diastolic dysfunction is Ventricular interdependence[33].The ventricles even though are separated are connected anatomically and functionally in both series and parallel.

The pulmonary circulation provides the serial connection hence loading conditions of one ventricle. common anatomical structures like interventricular septum,pericardium and muscle fibres maintain the parallel connection between the ventricles.This results in ventricular interdependence during systole and diastole. In our study there was a statistically significant correlation between several diastolic indexes of left ventricle and right ventricle. There is significant correlation between right ventricle E/A ratio and left ventricle E/A ratio and left ventricular deceleration time of E wave. There is also significant correlation between right ventricle deceleration time of E wave and left ventricle E/A ratio Right ventricular hypertrophy can be seen in more than 50% of patients with HCM[33].

The disarray of myocardial fibres in hypertrophic cardiomyopathy is not limited to the left ventricle but also affects the right ventricle . Hence the right ventricular diastolic dysfunction observed in hypertrophic cardiomyopathy in all our patients may be contributed by the disarray of myocardial fibres rather than the severity of right ventricular hypertrophy.

RISK STRATIFICATION OF HCM

Family H/O Sudden cardiac death

Family H/O sudden cardiac death was present in 27.5% of patients with HCM.This is in contrast to a study by Maron et al where 10-20% had a family H/O sudden cardiac death and 5 % had more than two sudden cardiac deaths in the family which suggests a malignant form of HCM[34]. 66.7% of patients with Maron Type II had a family history of sudden cardiac death.20% of patients with Maron Type III had a family history of sudden cardiac death and 25 % of patients with Maron Type II had a family history of sudden cardiac death.

Maximum LV Wall thickness

No patient had a maximum LV wall thickness of greater than 30 mm.This is in contrast to study by Maron et al where maximum LV wall thickness of greater than 30 mm was seen in < 3% of patients[35].spirito et al and olivetto etal have found that maximum LV wall thickness of greater than 30 mm is a sudden cardiac death risk factor mainly in younger patients[32].

Non-sustained ventricular tachycardia

Non-sustained ventricular tachycardia as detected by 24hrs Holter study was present in 25% of patients with HCM.This is similar to study by Monserrat et al where 19.6% of patients had NSVT[36].They have concluded that sudden cardiac death is significantly increased in young patients with HCM and NSVT. Non-sustained ventricular tachycardia as detected by 24hrs Holter study was present in 26.7% of type III Maron HCM patients.. Non-sustained ventricular tachycardia as detected by 24hrs Holter study was present in 37.5 % of type IV Maron HCM patients.

SYNCOPE

Syncope was seen in 52.5% of all patients with HCM. Syncope was seen in 66.7% of patients with Maron Type I and II. Syncope was seen in 40 % of patients with Maron Type III and 56.25% patients with Maron type IV.This is similar to a study by Maron et al where syncope was seen in greater than 50% of patients and where syncope was the only marker in more than one third of patients[35].

Study limitations

1. Our study evaluated only the prevalence among patients referred for echocardiography and not among the community.

2. Our study evaluated the patients during the time period of the study,rather than those who were first diagnosed.

3. Provocative tests were not standardized and was not attempted in all patients.

4. Many patients were on medications, which might alter the measured LV outflow gradient during the study or might have even abolished such a gradient in some and thus the prevalence of the obstructive type of HCM may have been underestimated.

CONCLUSION

1. Majority of patients were in Type III and Type IV of Maron classification of hypertrophic cardiomyopathy .
2. Syncope was the most common sudden cardiac death risk factor seen in our study.
3. Maximum LV wall thickness of greater than 30 mm , a sudden cardiac death risk factor was not present in our study.
4. There was no statistically significant relationship between myocardial tissue Doppler velocities of obstructive and non-obstructive HCM.
5. There was no statistically significant relationship between pulse Doppler mitral inflow velocities of obstructive and non-obstructive HCM.
6. Biventricular diastolic dysfunction is seen in most patients with HCM.
7. Right ventricular diastolic dysfunction may be contributed by the disarray of myocardial fibres rather than the severity of right ventricular hypertrophy
8. There is a significant correlation between several right ventricular and left ventricular diastolic parameters

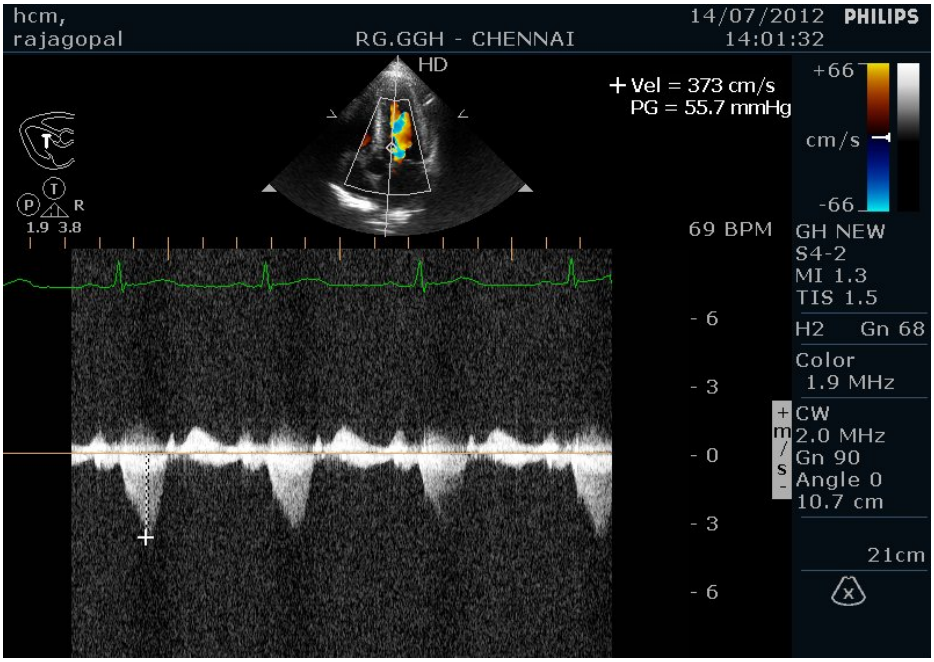


Figure A : shows measurement of LVOT gradient in HCM

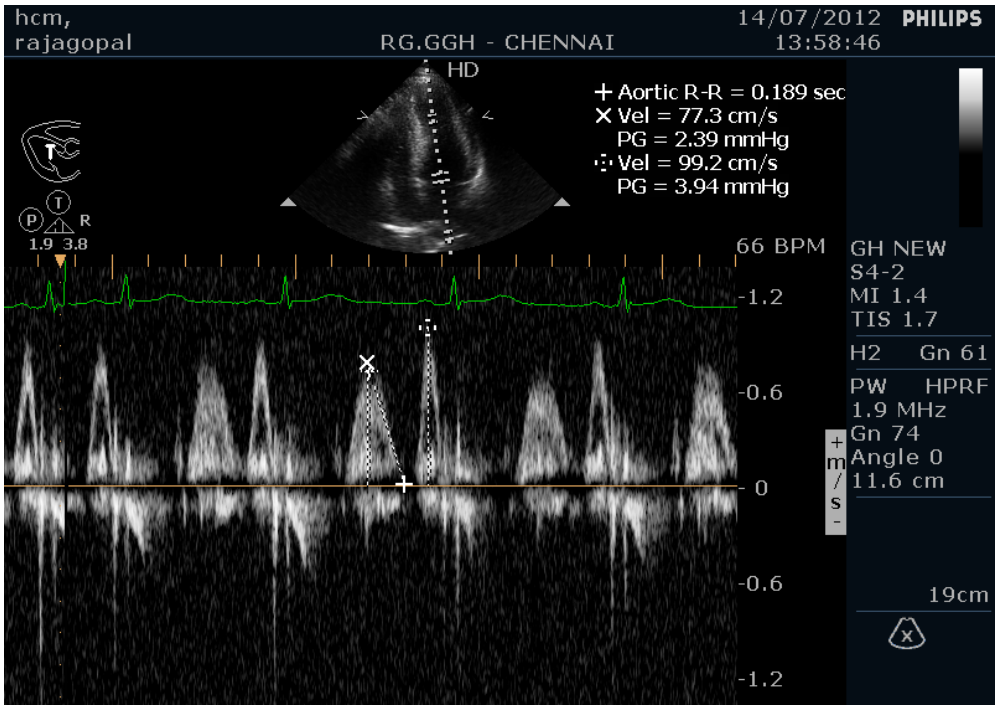


Figure B:shows Mitral inflow pulse wave Doppler tracing

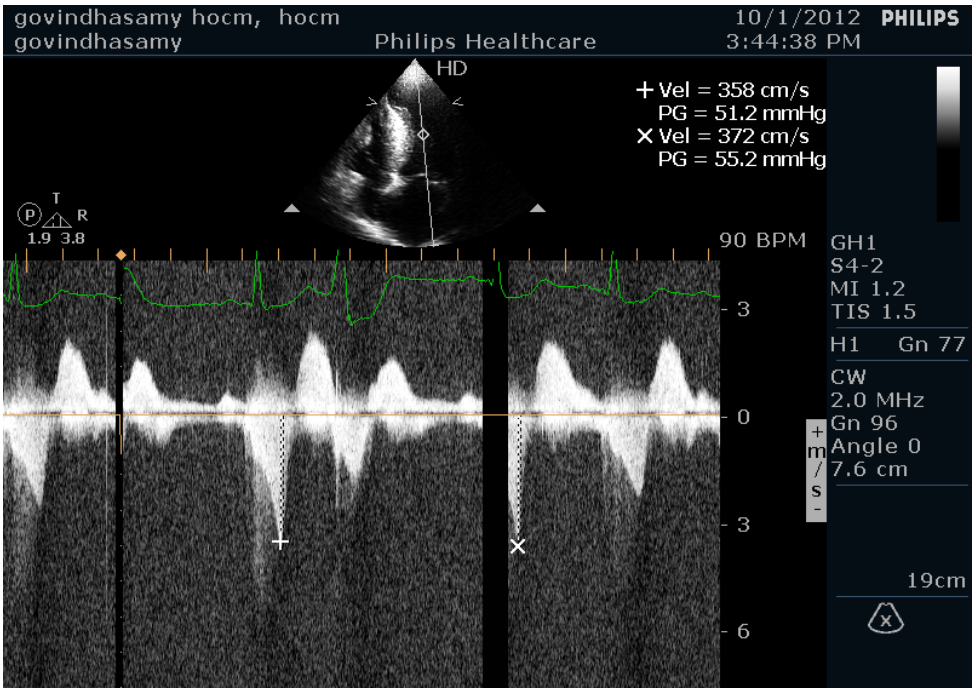


Fig.C showing LVOT gradient with dagger-shaped appearance

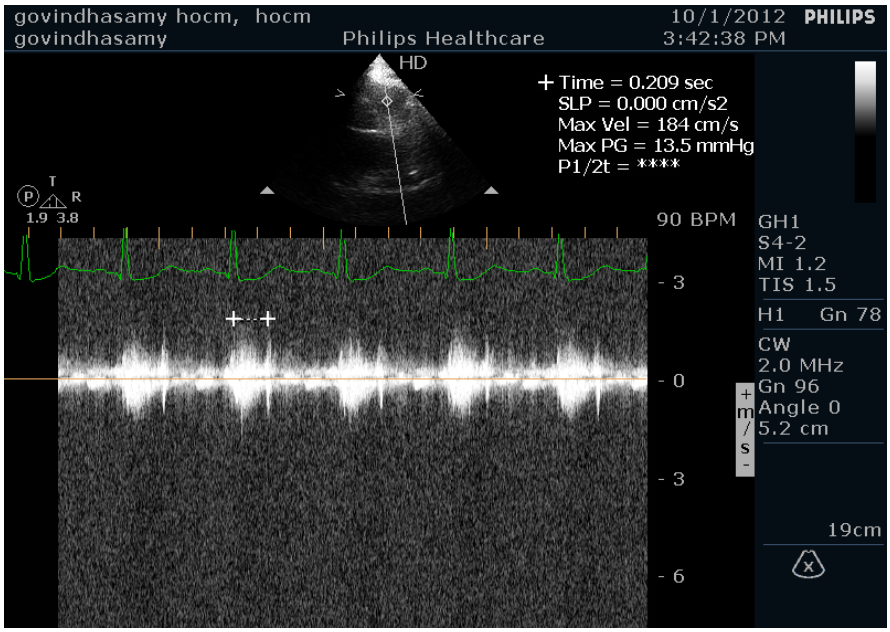


Figure.D showing measurement of RP interval

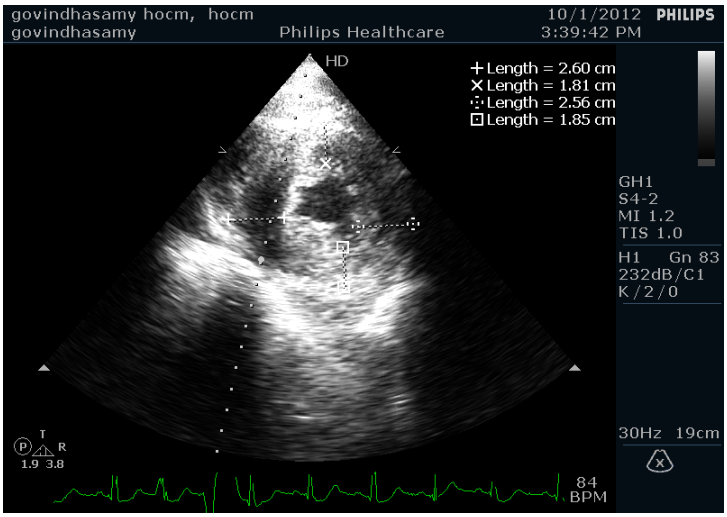


Fig.E showing categorization of HCM according to Maron types

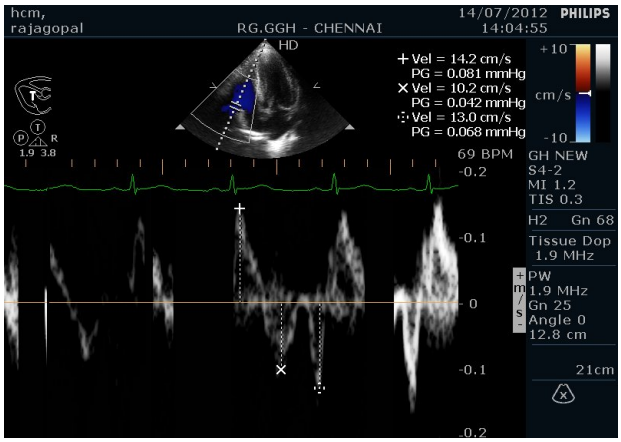


Fig.F showing TDI at tricuspid lateral annulus for assessment of RV diastolic function

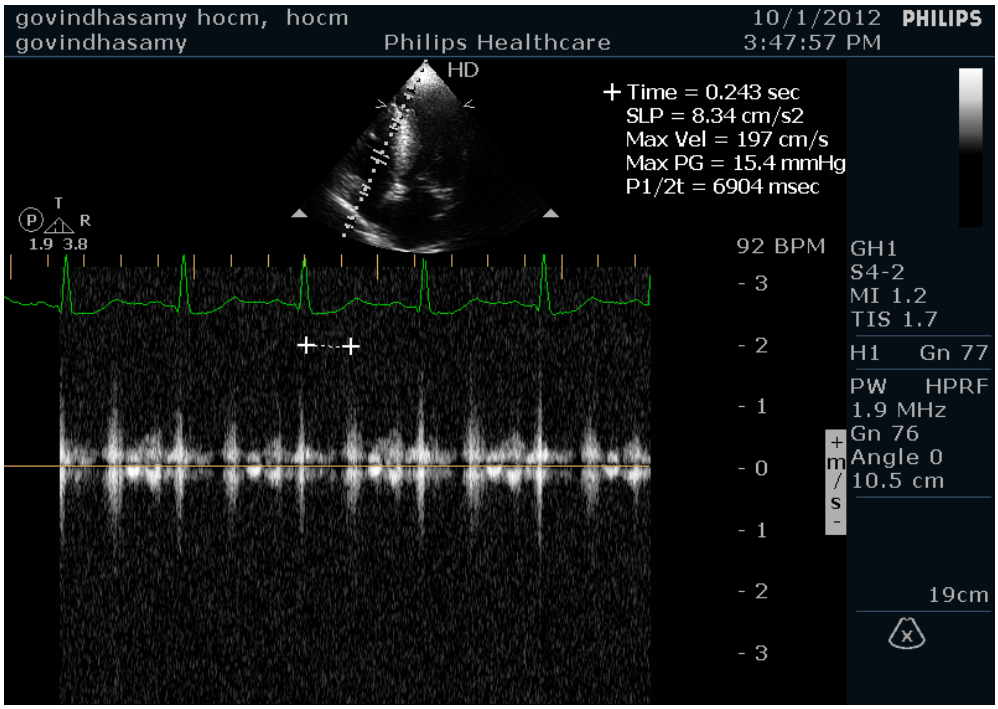


Fig.G showing measurement of RT interval

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ACRONYMS & ABBREVIATIONS

HCM	-	Hypertrophic cardiomyopathy
LVEDP	-	Left Ventricular End Diastolic pressure
LVOT	-	Left Ventricular Outflow Tract
DDD	-	Dual Chamber Pacing
ICD	-	Implantable Cardioverter Defibrillator
WPW	-	Wolf Parkinson White Syndrome
SAM	-	Systolic Anterior Motion
BOE	-	Breathlessness On Exertion
NSVT	-	Non Sustained Ventricular Tachycardia
S D	-	Standard deviation
ACC	-	American College of Cardiology
AHA	-	American Heart Association

PROFORMA

Name :

Age :

Sex :

Address :

CD No. :

SYMPTOMS :
No symptoms:
Chest pain:
SOB Class:
Palpitations
Syncope

Risk Factors

Hypertension Diabetes Mellitus

Smoking Family History

Menopause

Past History :

Treatment History

Physical Examination

1. General Examination

2. Vital Signs

B.P

Pulse

Respiration JVP Height cm Waveform

3. Systemic Examination

CVS

Inspection / Palpation

Apex Parasternal Heave

Palpable Sounds Thrills

Auscultation

S1 S2 Murmurs

Extra Heart Sounds

Other System

RS: PA: CNS :

ECHOCARDIOGRAPHIC ASSESSMENT OF HCM

Name: Age: Sex:

Echocardiographic parameters:

M-mode:

LV: EDD- ESD- EF- FS-

Septal thickness

Posterior wall thickness

RV: RVFWT RVEDD

Mitral valve:

Aortic valve: LVOT diameter:

LA :

Tricuspid valve:

Pulmonary valve:

RVOT : MPA:

2 D and DOPPLER HEMODYNAMIC ASSESSMENT:

Mitral inflow:

E-wave: Peak velocity - DT-
A-wave: Peak velocity - TVI-
E/A ratio:
TISSUE DOPPLER
Mitral annular: E' velocity- A' velocity-
E/E' ratio:
SAM Grade :
MR :
Aortic Outflow:

LVOT GRADIENT:
AORTIC Peak velocity:

VTI:

IVRT:

IVCT:
Tricuspid inflow:

E-wave: Peak velocity- DT-
A-wave: Peak velocity- TVI-

RT interval

RV Outflow
Pulmonary valve: Peak velocity

RP interval

RV IVRT

Pattern of Hypertrophy :

PATIENT CONSENT FORM

STUDY TITLE :

Risk stratification of patients with Hypertrophic Cardiomyopathy and assessment of Biventricular diastolic function by pulse/tissue doppler echocardiographic imaging ”

PARTICIPANT NAME : **DATE:**

AGE: **SEX:** **I.P.NO. :**

The details of the study have been provided to me in writing and explained to me in my own language.

I confirm that I have understood the purpose of the above study. ☐

I have the opportunity to ask the question and all my questions and doubts have been answered to my complete satisfaction. ☐

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving any reason, without my legal rights being affected. ☐

I understand that investigator, the institution, regulatory authorities and the ethical committee will not need my permission to look at my health records both in respect to the current study and any further research that may be conducted in relation to it, even if I withdraw from the study. I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ☐

I hereby consent to,undergo complete physical examination ,and diagnostic tests including hematological, biochemical, radiological and urine examinations ☐

I have been given an information sheet giving details of the study . I hereby consent to participate in the above study ☐

Signature of the Participant

Information to Participants

Title: Risk Stratification Of Patients With Hypertrophic Cardiomyopathy And Assessment Of Biventricular Diastolic Function By Pulse/Tissue Doppler Echocardiographic Imaging

Principal Investigator: DR.A.MURALIDHARAN

Co-Investigator(if any):

Name of Participant:

Site : RGGGH& MMC, Chennai

You are invited to take part in this research/ study/procedures/tests. The information in this document is meant to help you decide whether or not to take part. Please feel free to ask if you have any queries or concerns.

What is the purpose of research?

Hypertrophic cardiomyopathy (HCM) is a genetically transmitted disease with broad morphologic and clinical spectrum. Patients with hypertrophic cardiomyopathy are mostly discovered during routine examination, because of ECG abnormalities, or when they become symptomatic. Echocardiography remains the corner stone for its diagnosis and classification.HCM is the most common cause of sudden death in young.Hence we aim to stratify the risk of SCD in HCM patients . Left ventricular diastolic function in hypertrophic cardiomyopathy seems to be well studied but little is known about right ventricular diastolic function in hypertrophic cardiomyopathy. Right ventricular hypertrophy and elevated right ventricular end diastolic pressures have been reported in patients with hypertrophic cardiomyopathy. On the other hand the two ventricles are in anatomic and functional connection, hence the loadingconditions of one ventricle may affect the function of the other.Hence Biventricular diastolic function is evaluated using pulse and tissue doppler echocardiography. We have obtained permission from the Institutional Ethics Committee.

The study design: It is a Prospective observational study

Study Procedures The study involves risk stratification of patients with hypertrophic cardiomyopathy and assessment of biventricular diastolic function by pulse/tissue doppler echocardiographic imaging

Confidentiality of the information obtained from you

You have the right to confidentiality regarding the privacy of your medical information (personal details, results of physical examinations, investigations, and your medical history). By signing this document, you will be allowing the research team investigators, other study personnel, sponsors, Institutional Ethics Committee and any person or agency required by law like the Drug Controller General of India to view your data, if required.The information from this study, if published in scientific journals or presented at scientific meetings,will not reveal your identity.

How will your decision to not participate in the study affect you?

Your decision not to participate in this research study will not affect your medical care or your relationship with the investigator or the institution. You will be taken care of and you will not loose any benefits to which you are entitled.

Can you decide to stop participating in the study once you start?

The participation in this research is purely voluntary and you have the right to withdraw from this study at any time during the course of the study without giving any reasons. However, it is advisable that you talk to the research team prior to stopping the treatment/discontinuing of procedures etc.

Signature of Investigator Signature of Participant

Date :

S.NO	NAME	AGE	SEX	LVEDD	LVESD	LVEF	FS	SEPTAL THICKNESS	PW THICKNESS	RVFWT	RVEDD	LV-PVE	LV-PVA	LV- E/A	LV-DTE	RV-PVE
1	abdul jalil	54	m	38	25	63	34	21	9	7	20	57	72	0.8	223	45
2	achuthan	36	m	47	32	61	32	16.4	9.6	6.7	26	86.6	54.4	1.6	148	72.6
3	arumugam	65	m	40	23	65	35	16.6	10.6	5.16	22.8	105	63.5	1.65	189	41.9
4	madhuram	52	m	41	27	64	34.2	18	10.5	9	16.6	76	69	1.1	155	69.9
5	malleswari	25	f	36	18	82	50	18.9	10.2	8.6	24.5	77.5	55.1	1.4	115	60
6	arulmoorth	52	m	42	28	62	33	17.8	7.8	5.2	16.8	64.8	77.6	0.8	236	42.6
7	saravanan	37	m	46	22	80	52	16.8	8.8	5.7	27	88.5	48	1.8	118	53.8
8	usha	44	f	45	23	77	48	18.1	7.3	6.9	21.7	110	145	0.75	219	47.5
9	sankar	40	m	40	28	58	30	14	6.7	5.7	18.1	122	88	1.38	148	67.8
10	suresh	56	m	42	27	65	36	17.6	8.2	5.3	16.4	36	53	0.7	167	30
11	murugan	45	m	37	22	65	35	16.6	10.6	5.9	25.1	46.4	41.5	1.1	148	47.8
12	parameswa	60	f	44	24	75	45.5	16.3	6.8	5.7	21.8	99.1	65.6	1.5	266	55.8
13	govindasar	50	m	45.8	27.5	69	40	21	11	8	22	188	76.4	2.4	135	62
14	rajivgandhi	38	m	46.7	33.2	57	28	15	6.2	7.7	24	57.5	41.5	1.4	148	64
15	ramachandran	32	m	39	20	77	49	14.9	9	5.2	23	126	84.1	1.5	229	98.2
16	smriti	36	f	47	25	76	47	15.4	8.9	7.8	27.7	74.2	97.3	0.8	178	49.8
17	thirumoort	40	m	45	24	76	47	21.8	9.8	7.8	25	48.5	40.4	1.2	261	42.4
18	balu	52	m	42	25	70	40	16	9	5.3	18	83	112	0.7	130	40
19	anish	30	m	42	18	70	57	16.5	7.1	6.2	23	77	92	0.8	186	60
20	arulpandi	38	m	44	22	79	50	20	11.2	8.5	22.4	76.4	54.3	1.4	121	64
21	senthilkum	37	m	47	29	68	38	18.8	8.1	5.7	17.6	62.8	79.6	0.78	256	46.8
22	sivakumar	40	m	47	21	82	54	18.8	10.1	6.7	17.8	93.5	51	1.8	121	55.8
23	sudha	30	f	35	23	63	34	17.1	8.3	7.9	19.8	109	155	0.7	229	45.5
24	sudhakar	42	m	43	28	64	35	13	6.7	6.7	17.1	112	68.4	1.6	148	69.8
25	krishnamo	48	m	30	17	77	44	16.5	9.2	5.6	14.4	34	51	0.66	170	32
26	elumalai	42	m	39	22	73	44	15.5	10.3	5.6	23.2	47.8	42.5	1.1	144	49.2
27	shruti	26	f	44	21	80	52	16.7	6.5	5.4	22.7	98.6	63.4	1.5	262	53.7
28	kamal	33	m	44.7	27	69	39	22	12	7.6	24	178	76.2	2.3	128	66
29	lakshmipat	45	m	45.8	31	61	32	13	6.6	7.2	22	54.3	42.7	1.3	145	60
30	ahamed	41	m	42	23	74	45	16.2	9.6	5.7	21.3	110	62.6	1.75	178	43
31	rajagopal	65	m	49	25	65	35	16.2	9.9	8.4	28.7	77.3	99.2	0.8	189	51.8
32	vellachi	55	f	35	24	65	35	20.7	9.6	8.2	24	46.4	41.5	1.1	271	40.3
33	venkatesh	52	m	41	25	69	38	14	9	5.7	16	86	102	0.8	133	42
34	viji	22	f	32	18	65	35	14.5	7.2	6.7	25	78	99	0.8	182	62
35	saroja	33	f	46	24	77	48	22	10.1	6.8	22	59	74	0.8	212	43
36	joseph	28	m	47	23	79	51	16.9	9.3	6.3	28	89.9	53.2	1.7	152	71.7
37	jeagan	45	m	44	21	80	52	16.8	10.1	5.2	23.2	107	68.2	1.6	178	42.8
38	sundar	46	m	41	24	71	41	17	9.2	7	22	74	65	1.1	152	67.8
39	jyotikumar	32	m	39	17	84	56	18.6	9.8	8.2	22.5	73.5	52.5	1.4	120	62
40	sivan	30	m	44.2	27.2	68	38	20	9	7	21	176	74.2	2.4	132	64

RV-PVA	RV-E/A	RV-DTE	MV-Ea	MV-Aa	TV-Ea	TV-Aa	FAMILY H/O SCD	syncope	NSVT-HOLTER	SAM	MR	LVOT GR	E/Ea	Maron type	RV-IVRT
48	0.9	243	3.3	6.9	45.3	48.5	x	x				170/11.6	17.3	2	94
49.6	1.46	121	7.1	4.5	7.6	33.7	x	x	vpc,1stdegreeavblock	Gr1	1+	106/4.6	12	2	127
30.7	1.36	236	10.1	5.9	16.4	16.3	x	x		Gr2	1+	138/7.62	10.3	4	170
65.5	1.06	202	4.3	6.6	5.9	8.4			vpc			150/9.4	17.6	3	139
34	1.7	202	6.7	4.9	16.8	15.5						108/4.8	11.6	4	240
32.5	1.3	240	6	8.1	7.5	12.7						106/4	12.6	1	68
33.5	1.6	246	8.5	4.1	8.5	4.1						110/5	10.4	2	102
34	1.4	192	4.8	7.7	12.7	23.4	x	x	nsvt	Gr3		440/77	23	3	77
32.6	2.1	159	9.7	7.5	23.8	15.6						110/5	10.4	4	86
41	0.7	120	5	8	7	11						112/5	7.2	3	78
43.8	1.09	277	3.72	4.19	13.4	18.8				Gr2		140/7.87	12.4	3	140
41.2	1.3	302	3.3	5	14.3	11.1			vpcs	Gr2		249/24.8	33	3	74
60	1.03	101	7.3	9.7	11	17			nsvt	Gr3	2+	331/43.7	25.7	4	134
40	1.6	223	4.3	6.6	8.7	16.3						84.4/2.85	13.37	4	248
119	0.8	115	6.1	9	15.3	26.1	x	x	nsvt	Gr2	2+	468/87.5	20.6	4	249
54	0.9	276	4.9	7.7	11.1	13.4		x	nsvt	Gr3	1+	368/54	15.1	4	76
47.6	0.9	124	2.3	4.8	11	31		x				122/6	21	1	220
45	0.9	260	5.6	8.1	5.7	8.2		x	vpcs	Gr1	1+	289/33	14.8	3	272
58	1	178	2.6	4.2	11	31		x	nsvt	Gr2	2+	549/121	29.6	3	70
30	2.1	210	5.5	4.2	14.7	16.2						120/6	13.9	4	250
33.5	1.4	270	5	9.1	9.5	13.8						106/4.6	12.6	3	68
35.6	1.6	256	9.5	4.3	9.5	4.3						119/5.69	9.8	2	93
36	1.3	202	5.8	8.7	14.7	25.4	x	x	nsvt	Gr3		463/85.6	18.8	3	67
35.6	1.9	169	10.7	9.5	21.8	18.6						120/5.7	10.5	4	88
42	0.7	110	6	8	9	13						104/4.3		3	78
41.8	1.2	274	3.42	4.1	12.7	17.5				Gr2		130/7	14	3	138
40.4	1.3	288	3.5	6	13.7	10.9			vpc	Gr2		279/32	28	3	72
60	1.1	111	7.5	9.4	12	18			nsvt	Gr3	2+	351/49	24	4	138
45	1.3	211	4.2	6.9	8.3	16.6						94.4/3	13	4	232
31.6	1.3	228	11.1	5.6	16.6	17.3	x	x		Gr2	1+	148/9	10.6	4	168
56	0.9	297	4.7	7.6	10.2	13		x	nsvt	Gr3	1+	358/51.8	16.4	4	70
46.8	0.9	121	2.2	4.5	13	32		x				133/7	21	1	240
47	0.9	270	5.9	8.4	5.9	8.4		x	vpcs	Gr1	1+	279/31	14.5	3	270
61	1	182	2.2	4.5	13	32		x	nsvt	Gr2	2+	569/130	35	3	64
47	0.9	233	3.1	6.7	40.2	46.4	x	x				176/12	19	2	98
48.3	1.5	124	6.7	4.2	7.2	31	x	x	vpc,1stdegreeavblock	Gr1	1+	103/4	13	2	123
28.9	1.5	239	10.6	5.6	16.2	16.3	x	x		Gr2	1+	128/7	10	4	170
63.2	1.1	201	4.4	6.8	5.7	8.1						143/8	16.8	3	132
30	2	210	6.4	4.7	15.9	14.2						102/4	11.5	4	270
59	1.1	110	7.1	9.5	12	19			nsvt	Gr3	2+	343/50	24.8	4	137

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

Telephone No : 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr. A. Muralidharan
PG in DM Cardiology
Madras Medical College, Chennai -3

Dear Dr. A. Muralidharan

The Institutional Ethics committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled "Risk stratification of patients with Hypertrophic Cardiomyopathy and assessment of Biventricular diastolic function by pulse / tissue Doppler echocardiographic imaging " No.30082012.

The following members of Ethics Committee were present in the meeting held on 10/08/2012 conducted at Madras Medical College, Chennai -3.

1. Dr. S.K. Rajan. M.D.,FRCP.,DSc	-- Chairperson
2. Prof. Pregna B. Dolia MD Vice Principal, Madras Medical College, Chennai -3 Director , Institute of Biochemistry, MMC, Ch-3	-- Member Secretary
3. Prof. B. Vasanthi MD Prof of Pharmacology ,MMC, Ch-3	-- Member
4. Prof. C. Rajendiran, MD Director , Inst. Of Internal Medicine, MMC, Ch-3	-- Member
5. Prof. S. Deivanayagam MS Prof of Surgery, MMC, Ch-3	-- Member
6. Thiru. S. Govindsamy. BABL	-- Lawyer
7. Tmt. Arnold Soulina MA MSW	-- Social Scientist

We approve the proposal to be conducted in its presented form.

Sd/ Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

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Assignment title	Medical
Author	Muralidharan Azhakesan 16101507 D.M. Cardiology
E-mail	drmurali75@gmail.com
Submission time	24-Mar-2013 05:11PM
Total words	8207

First 100 words of your submission

“RISK STRATIFICATION OF PATIENTS WITH HYPERTROPHIC CARDIOMYOPATHY AND ASSESSMENT OF BIVENTRICULAR DIASTOLIC FUNCTION BY PULSE/TISSUE DOPPLER ECHOCARDIOGRAPHIC IMAGING” Dissertation submitted for D.M. DEGREE EXAMINATION BRANCH II – CARDIOLOGY MADRAS MEDICAL COLLEGE AND GOVERNMENT GENERAL HOSPITAL CHENNAI – 600 003 INTRODUCTION Hypertrophic cardiomyopathy is a common autosomal dominant cardiovascular disease . Dynamic obstruction to LV outflow can occur under resting or physiologically provocable conditions in patients with HCM. various phenotypic and genotypic heterogeneity are observed in HCM. HCM is the most common genetically transmitted cardiovascular disease which affects 1 in 500 people...

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"RISK STRATIFICATION OF PATIENTS WITH HYPERTROPHIC CARDIOMYOPATHY AND ASSESSMENT OF BIVENTRICULAR DIASTOLIC FUNCTION BY PULSE/TISSUE DOPPLER ECHOCARDIOGRAPHIC IMAGING"

Dissertation submitted for
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MADRAS MEDICAL COLLEGE
AND GOVERNMENT GENERAL HOSPITAL
CHENNAI – 600 003